



# What We Have Learned—Milestones in Pediatric Contact Dermatitis

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## Abstract

**Purpose of Review** This review highlights recent developments in the field of pediatric allergic contact dermatitis (ACD) and patch testing. We will review updates on the pathophysiology of contact dermatitis, discuss new contact allergens, explore the impact of dupilumab on patch testing, and provide pearls for the diagnosis and management of ACD in children.

**Recent Findings** ACD is not a single immunologic phenomenon but rather has contributions from multiple inflammatory pathways. Emerging contact allergens include ingredients found in “slime” toys, glucose monitors and insulin pumps, and electronic equipment. Data thus far suggests that patch testing results are generally reliable in the face of concurrent dupilumab use.

**Summary** ACD is likely underrecognized and underdiagnosed in pediatric patients, including infants and young children. Providers should keep patient-specific factors and emerging trends in mind when addressing suspected ACD, consider contact dermatitis when they encounter challenging cases of atypical, refractory, or chronic dermatitis, and feel comfortable performing patch testing in children.

**Keywords** Pediatric allergic contact dermatitis · Irritant contact dermatitis · Patch testing · Pediatric allergens

## Introduction

Contact dermatitis is a common inflammatory skin disease, the etiology of which can be categorized as allergic or irritant. While irritant contact dermatitis is understood to widely affect children, it is a common and historical misconception that allergic contact dermatitis (ACD) is rare in children. As this article aims to highlight, ACD is relatively prevalent in the pediatric population. Patients with contact dermatitis may also have a concomitant primary dermatitis, such as atopic dermatitis, which can make the diagnosis of

contact dermatitis even more challenging to reveal. Both pediatric and adult dermatologists should be able to recognize the prevalence, patterns, and allergens/irritants relevant to the pediatric population. This knowledge can significantly impact clinical management in children with atypical, treatment refractory, and/or chronic dermatitis.

Here, we will briefly review the latest data from the past 5 years concerning contact dermatitis in the pediatric patient, with a focus on ACD, including the most common and emerging contact allergens relevant to children, specific nuances of patch testing, and prevention strategies. We will also review the evolving role tele-dermatology may play in the future diagnosis and management of contact dermatitis.

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## Pediatric Irritant vs. Allergic Contact Dermatitis

There are two forms of contact dermatitis, irritant contact dermatitis (ICD) and ACD. ICD, which is caused by direct injury to the skin by an irritating or toxic substance, does not require prior sensitization and will develop in any individual with sufficient concentration and exposure time. This injury activates the innate immune system and results in an

inflammatory response [1]. ICD is a more frequent cause of contact dermatitis than ACD, accounting for approximately 80% of cases [1]. Unlike ACD, ICD usually remains confined to the specific anatomic location of injury.

Examples of irritant dermatitis specific to children include perineal dermatitis from soiled diapers, perioral dermatitis from saliva, and hand dermatitis secondary to washing or sanitizers [2••]. During the COVID-19 pandemic, the American Contact Dermatitis Society (ACDS) published recommendations for hand hygiene recognizing the important balance between infection prevention and dermatitis. Overall, alcohol-based hand sanitizers with moisturizers were recommended given the decreased risk for sensitization and irritation when compared with soaps and detergents [3].

In contrast to ICD, ACD is a type IV delayed-type hypersensitivity reaction, which occurs in two phases: sensitization and elicitation. The sensitization phase occurs when allergens cross the epidermal barrier and are encountered by Langerhans cells or dermal dendritic cells which recognize them as foreign [1]. These antigen-presenting cells then migrate to regional lymph nodes where naïve T-cells are activated, resulting in proliferation of allergen-specific T-cells in the peripheral circulation [1, 4]. In the subsequent elicitation phase, an allergen again contacts the skin and a sensitized specific T-cell recognizes it and activates the inflammatory response that ultimately leads to skin symptoms at the site of exposure [1, 4]. In ACD, the dermatitis can expand outside the confines of initial contact, and there may be hours to days between the contact and development of symptoms [5•].

For many years, it was believed that ACD was a  $T_H1$ -skewed immune response. A study by Dhingra et al. looked at the molecular and cellular profiles of patch tested skin and demonstrated differential immune responses induced by different allergens [6•]. For example, fragrance induced expression of  $T_H2$ -related genes, whereas nickel induced  $T_H17$ - and  $T_H1$ -related genes [6•]. Although the exact mechanisms are not well understood, it is now accepted that ACD is not a single immunologic phenomenon, but rather has contributions from multiple pathways, including  $T_H1$ ,  $T_H2$ ,  $T_H17$ , and  $T_H22$  [6•].

## Pediatric Allergic Contact Dermatitis

ACD has previously been described as an uncommon occurrence in children, and however, more recent data suggests prevalence rates of 16.5% (or higher), as compared with 21.4% in adults [2••, 4, 7–10]. Recent studies have found that positive patch test (PPT) rates in the pediatric population are comparable to adults, with up to 65% of pediatric patients referred for patch testing having one or more positive reactions, half of which are clinically relevant [2••,

11•]. Contributing factors for allergen exposures in children include cleansing and bathing habits, dressing habits, exposure to jewelry and other metals, personal care products, outdoor and indoor activities, and relevant history of other dermatological conditions such as atopic dermatitis. There are overall lower rates of patch testing done in the pediatric population compared to adults, suggesting decreased referral rates for patch testing and potentially underdiagnosis [2••, 12].

Etiologies of ACD in children are very diverse – important considerations include medications, personal care products, toys, sports, activities, and hobbies, as well as products used by parents and caregivers. The top allergens in children have been described consistently in numerous registries and reviews, and are summarized in Table 1 [2••, 11•, 13].

## Nickel

Nickel is omnipresent in our world and is the most common clinically relevant PPT in both children and adults. Nickel is responsible for up to 24% of PPTs in children (ranges of 8–28%), of which 69% are clinically relevant [14•]. Items containing nickel include coins, jewelry, toys, cellphones, computer parts, video game consoles, paints, musical instruments, belts, and clothing. Nickel can also be present in food and may cause systemic contact dermatitis. The most relevant nickel in ACD is “free nickel,” or the amount of nickel released from a product [14•]. Female pediatric patients are 50% more likely to have a PPT against nickel, likely due to early jewelry exposure. Nickel sensitivity is also correlated with total number of piercings in both males and females [15]. In 1994, European regulations were put in place to control the amount of nickel in consumer products. European countries that adopted nickel regulations in the early 1990s have saved an estimated \$2 billion in healthcare costs due to nickel contact dermatitis. Similar regulations have not been implemented in the United States (US) [14•]. In 2011, after the development of the nickel workgroup and resolutions adopted by the American Academy of Dermatology (AAD),

**Table 1** Top pediatric contact allergens in the United States

Category	Allergen
Metals	Nickel, cobalt
Fragrances	Fragrance mix I & II, balsam of Peru
Emollients/surfactants	Propylene glycol, cocamidopropyl betaine, lanolin
Topical antibiotics	Bacitracin, neomycin
Preservatives	MCI/MI, MI, formaldehyde (releasers)

Adapted from Neale et al. [2••, 50••]

*MCI/MI* methylchloroisothiazolinone/methylisothiazolinone, *MI* methylisothiazolinone

the American Society for Testing and Materials (ASTM) adopted a voluntary safety standard for nickel, and however, many companies have yet to adopt these guidelines [14•]. More recently, in 2015, the Nickel Allergy Alliance was created and, in conjunction with the AAD, continues to push for mandatory regulations of nickel in the US. They suggest that with further regulation of nickel in products, there is a potential avoidance of \$5.7 billion per year in healthcare costs related to nickel dermatitis [14•].

## Cobalt

Cobalt is another metal that is a repeated cause of ACD in the pediatric population. It is compounded with nickel and patients are often co-sensitized to both after exposure to metal-plated items including jewelry, toys, and clothing items. Rarely children can develop ACD to cobalt alone [2••]. Other potential exposures in the pediatric population include blue/green crayons and paints (as cobalt is often used as a pigment) and leather items, including shoes [7].

## Fragrance

Fragrances are some of the top contact allergens in the pediatric population. Fragrance allergy is commonly screened for using fragrance mix I/II and balsam of Peru (BoP), although this is a large category including numerous different allergens [2••, 4]. Exposure often occurs with personal care products, detergents, and perfumes (which can be by proxy from a parent/caregiver/sibling) [16]. Fragrance can also be used as “masking” fragrance to mask a product’s unpleasant smell for an overall neutral smell. Recent studies have found that cosmetic products marketed toward babies and infants and labeled as “hypoallergenic” and even “fragrance-free” often contained fragrances [16, 17]. Unfortunately, in North America, personal care product labels are not required to list anything more specific than “fragrance” or “parfum,” thus sensitized patients have to practice broad avoidance of all products containing fragrance.

## Formaldehyde and Formaldehyde Releasers

Formaldehyde itself is no longer used in personal care products in the European Union however can still be found in some products in the US and is a common allergen in the pediatric population. While “formaldehyde” will never be included in the ingredients list, a number of formaldehyde-releasing preservatives, including quaternium-15, imidazolidinyl urea, diazolidinyl urea, DMDM hydantoin, and Bronopol (2-bromo-2-nitropropane-1,3-diol), are found in personal care products and can be allergens as well. Bronopol is the most common of these preservatives to cause ACD in children [4].

## Methylchloroisothiazolinone/Methylisothiazolinone

Methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) is a preservative that is widely used in a variety of personal care products, paints, solvents, and cleaning products. The combination of MCI/MI has been a cause of ACD in personal care products for decades, though more recently, MI was introduced alone in much higher concentrations, which led to an increase in allergic contact diaper dermatitis due to its presence in baby wipes [18]. The European Union strictly regulated the use of these preservatives in consumer products, whereas no similar legislation has been enacted in North America. Nonetheless, it would seem manufacturers have taken notice, considering a recent study showing that nearly no popular, readily available baby wipes contain MI or other isothiazolinone derivatives [18]. However, MI is still used as a preservative in many personal care products marketed toward children, which supports data showing an increase in MI ACD from non-wet wipe products [18, 19]. In 2020, MI was reported as the culprit in ACD to children’s nail polish, as well as a cause of airborne contact dermatitis from a child’s water-based paint, household paint, and a cleaning product [20, 21]. MCI/MI is also a common source of “slime dermatitis,” which is discussed in greater detail below [22].

## Cocamidopropyl Betaine

Cocamidopropyl betaine (CAPB) is a surfactant commonly found in rinse-off products (shampoos, soaps, body washes) and has been described as a common yet underrecognized cause of ACD in children, with upward of 3% of children being reported as sensitized to the allergen [16, 23]. In one Polish study, CAPB was present in 30% of the analyzed 212 skin care products marketed for children 0–12 months of age [16]. It was also found to be an ingredient in a high proportion of “hypoallergenic” personal products for children [24]. Studies have also suggested a greater incidence of sensitization to CAPB in patients with atopic dermatitis [25].

## Lanolin

Lanolin is derived from sheep’s wool and is frequently used as an emollient in personal care products, with reports citing its presence in 9% of cosmetics [16]. Lanolin may cause ACD even in very young children, with sensitization rates cited at 1.2–6.2% of pediatric patch test patients [9, 23, 26]. Lanolin is a common allergen in those with atopic dermatitis likely due to their frequent and early exposure to emollients and skin care products [4, 9].

## Propylene Glycol

Propylene glycol (PG) is a synthetic alcohol commonly used as an emollient, emulsifier, solvent, and antimicrobial. It was named the ACDS Allergen of the Year in 2018 [27]. It is a common ingredient in cosmetic skin care products, topical medications (including steroid creams), household cleaners, and foods. It is both an irritant and a weak sensitizer, spurring debate as to which concentration and vehicle is ideal for patch testing, and calling into question the significance of positive patch test results [27]. PG is ubiquitous and was reported to be present in more than 37% of over 4500 products in the ACDS's 2016 Contact Allergen Management Program (CAMP) database [28]. According to the Pediatric Contact Dermatitis Registry (PCDR), of the 1142 US pediatric patch tests performed between 2015 and 2016, PG was the fifth most prevalent contact allergen, identified in 6.8% of children tested [27]. It is also a potential cause of rare cases of systemic contact dermatitis [27].

## Topical Antibiotics

Topical antibiotics, particularly neomycin and bacitracin, are frequently used for the treatment and prevention of superficial skin infections. These medications are readily available over the counter in the United States, thus contributing to high rates of sensitization in children [29]. Neomycin has been in the list of top pediatric allergens for several decades [29]. Topical antibiotics are known to cause delayed patch test reactions which can appear as late as 3 weeks, therefore, if suspicion is high, a delayed reading should be considered [30].

## ACD and Neonates/Infants

Previously, it was postulated that neonates were unlikely to develop ACD given their immature immune systems, but this has proven to be false. Neonates may be particularly vulnerable due to their decreased epidermal barriers and product exposures. With respect to the development of ACD, there are two prevalence peaks within early childhood, between 0–3 years and 6–7 years [11•].

Diaper dermatitis is a common skin condition of the neonate and can have numerous etiologies, the most common being ICD. Despite this, ACD is likely underrecognized and underdiagnosed in both diaper dermatitis and perineal dermatitis. It is hypothesized that the irritant dermatitis leading to skin breakdown in the perineal/diaper area can lead to increased risk of sensitization to allergens and subsequent ACD. Studies have found numerous allergens in diapers and diaper wipes [31•, 32]. While MCI/MI has largely been eliminated from wet wipes/diaper wipes, reports have

documented numerous other and emerging allergens [18]. Many products listed as “hypo-allergenic” or “safe for babies” contain allergens such as cocamidopropyl betaine, tocopherol, propylene glycol, fragrances, lanolin, Compositae family, and other botanical extracts, which have proven to be culprit allergens in diaper dermatitis due to ACD [32].

## ACD and Atopic Dermatitis

Atopic dermatitis (AD) is the most prevalent skin condition in the pediatric population. Its pathogenesis is multifactorial but is defined as a Th2-mediated disease commonly featuring mutations in filaggrin, leading to disruption of the epidermal barrier. ACD in the setting of AD has been explored extensively in the literature and the association of these conditions is controversial. For now, it seems that patients with AD have at least similar risk of developing ACD compared to non-AD patients. Several factors may put patients with AD at risk of ACD, including increased early sensitization to personal care products, decreased epidermal barrier function, and cross-over of Th2- to Th1-helper T-cells [5•].

Studies have found that patients with moderate-to-severe, uncontrolled AD often have more *false-negative* patch tests. It has been hypothesized that while AD is acute and active, the immune response is skewed toward a Th2 response, and however, once AD is controlled and in a more chronic phase, this leads to Th1 skewing, and more frequent PPTs. Additionally, patients with AD have an impaired skin barrier which results in greater absorption of potential allergens. Studies of moderate-to-severe AD patients showed more PPT to weaker allergens in personal care products as compared to healthy controls, suggesting increased absorption into the skin of those with AD [5•, 31•, 32].

A large review of the PCDR found that up to half of patients with ACD had a previous diagnosis of AD. Patients with AD were more likely to have been patch tested earlier in life, and were more likely to test positive to common allergens in personal care products including topical emollients [5•, 31•, 33]. In the PCDR study, Jacob et al. found the most common allergen in the AD patient population to be nickel, followed by fragrance mix and balsam of Peru, similar to the non-AD patient population. However, there were some notable differences compared to non-AD patients. AD patients were more likely to test positive to five allergens: CAPB, wool alcohol, lanolin, tixocortol pivalate (tester for corticosteroids class A which cross-reacts with class D2), and parthenolide. This is hypothesized to be due to early exposure to emollients and topical medications in the setting of treatment for AD. Interestingly, patients with AD had statistically significant lower rates of PPT to MCI/MI than non-AD patients. This may be secondary to MCI/MI's action as a potent sensitizer, which classically induces

a robust Th1 response, and may be dampened in those with a Th1/Th2 imbalance, as present in uncontrolled AD [31•].

## New Sources of Pediatric ACD

The COVID-19 pandemic has had lasting effects on all areas of medicine. With children spending significantly more time at home and parents inventing creative ways to entertain them, one can predict that various at-home activities may lead to upticks in ACD due to certain pediatric allergens. Emerging pediatric ACD trends over the past few years include slime dermatitis, gaming dermatitis, and dermatitis due to diabetes devices.

### Slime Dermatitis

Originally made famous by Slimer in the movie *Ghostbusters*, slime is a popular toy composed of a semi-viscous, sticky goo or gel, which in recent years has been popularized as a make-at-home activity for kids. Social media sites, including Instagram, YouTube, and TikTok, have made it easy to share slime recipes. In 2019, as autonomous sensory meridian response (ASMR) videos were popularized on these platforms, viewing slime videos became a popular trend. On TikTok alone, there are 15.9 billion views for the hashtag “slime.” Subsequently, slime dermatitis became an emerging pediatric ACD trend in 2017. Slime ingredients can vary based on the recipe but include both potential irritants and contact allergens. The base ingredients include a detergent, such as shampoo, soap, or laundry detergent, in addition to boric acid, which are both causes of ICD. Most slime recipes also include glue which can contain numerous contact allergens, including isothiazolinones [22, 34, 35]. A 2019 case report described the most common slime recipes on the internet and cited numerous other potential allergens, including propylene glycol, paraben mix, benzyl alcohol, cocamidopropyl betaine, triethanolamine, compositae mix, parthenolide, sesquiterpene lactone, diazolidinyl urea, DMDM hydantoin, sodium hydroxymethylglycinate, stearyl alcohol, cetearyl alcohol, cetyl alcohol, and tocopheryl acetate [22]. Of note, many of the potential allergens in slime are not present on the T.R.U.E. Test, but have been listed in the Pediatric Baseline Patch Test Series [22].

### Gaming/Electronics Dermatitis

Other potential allergen exposures during the COVID-19 pandemic include those related to increased electronic use, ranging from computers to tablets to cell phones. Video games that allow social interaction during this isolating period are more popular than ever. Many consoles and electronics contain nickel and other metals [14•]. There

are case reports of ACD due to cell phone use caused by high amounts of nickel released from the device and more recently isobornyl acrylate (IBOA) released from cell phone screen protectors in the occupational setting [36]. The literature also describes ACD in adults to computer mice, mouse pads, and keyboards, as these items often contain rubber compounds (i.e., dialkyl thiourea or neoprene) and various plastics. In 2018, a case was reported of a 12-year-old who developed an eczematous plaque at the site where his forearm rested on the metal hinge of his computer gaming desk, which was found to contain nickel [37]. We suspect upticks in these types of clinical presentations, which require detailed and thorough histories in the evaluation of the patient with suspected ACD.

### Diabetes Device Dermatitis

Treatment of type 1 diabetes mellitus (T1DM) in children has advanced significantly with the development of continuous subcutaneous insulin infusions (CSII), continuous glucose monitors (CGMs), flash glucose monitors (FGMs), and sensor augmented pumps (SAPs). Use of these devices has been shown to improve overall glycemic control [38].

However, with these new technologies has come a new wave of ACD. These systems require adhesives and prolonged skin contact time at sites of monitors and insulin pumps (sometimes up to 14 days). Dermatologic complications during T1DM management are not rare; it is estimated that anywhere between 33 and 90% of children using these devices develop skin rashes, including ACD [39, 40]. In children with T1DM using these devices, there is no known correlation between the development of ACD and duration of diabetes or degree of control of blood glucose levels [41].

Allergens found in diabetes devices include IBOA, ethyl cyanoacrylate, N,N-dimethylacrylamide (DMAA), and colophony (Table 2) [38–42]. IBOA is an acrylate highly utilized in medical devices as an adhesive. In the context of T1DM treatment, IBOA was found to be a component of the FreeStyle Libre glucose monitor’s housing, rather than the adhesive portion. Subsequently, the presence of IBOA was confirmed in several other glucose monitors and insulin pumps. In 2020, IBOA was selected as the ACDS Contact Allergen of the Year to raise awareness of its presence in medical devices and increasing rates of sensitization. Manufacturers of these systems have not often been forthcoming about the components of their sensors and monitors, though some have confirmed the presence of allergens within their devices. More recently, in the spring of 2019, the FreeStyle Libre 2 was introduced and marketed as IBOA free, suggesting that IBOA-sensitized patients may be able to use this device, and however, further observations are necessary [43]. They may also have the option to switch their CGM to Dexcom

**Table 2** Insulin pumps, glucose monitors, and relevant contact allergens

Brand (Manufacturer)	Device category	Reported allergen
Omnipod (Insulet)	CSII	IBOA, colophony
FreeStyle Libre (Abbott)	FGM	IBOA*, DMAA*
Dexcom G4 (Dexcom)	CGM	Ethyl cyanoacrylate
Dexcom G6 (Dexcom)	CGM	IBOA**
Enlite (Medtronic)	CGM	IBOA, DMAA, colophony

Hartsough and Hylwa [38], Lombardo et al. [41], Raison-Peyron et al. [42]

CSII continuous subcutaneous insulin infusion, FGM flash glucose monitor, CGM continuous glucose monitor, IBOA isobornyl acrylate, DMAA N,N-dimethylacrylamide

\* Absent from FreeStyle Libre 2

\*\* Absent from Dexcom G5

G4/G5 or Eversense; however, there is not a clear IBOA-free alternative to the Omnipod insulin pump. Colophony, DMAA, and ethyl cyanoacrylate are used in medical-grade adhesives and have also caused ACD related to diabetes devices.

Anecdotally, we have managed suspected ACD due to the Omnipod and Dexcom systems in our clinics. We currently recommend rotating the body site of application for both the CGM and CSII, while using topical corticosteroids to these sites after use, and preemptively using steroid-sparing agents, such as tacrolimus ointment, to sites for several days prior to use. We have attempted the use of barrier dressings such as Tegaderm (3 M, St. Paul, MN), Duoderm (ConvaTec, Oklahoma City, OK), and barrier film/spray/cream (Cavilon, 3 M, St. Paul, MN) beneath the site of monitor and/or sensor applications, however have run into difficulty with these devices then adhering appropriately to the skin. We have also attempted pre-device application of topical steroid foam, spray, solution, and oil of varying potencies without success due to same difficulty in subsequent adhesion of the diabetes device. Encouragingly, there are newer reports of patients successfully using hydrocolloid blister plaster beneath diabetes devices to prevent ACD from IBOA. These products (i.e., Hansaplast, Beiersdorf, Hamburg, Germany; Cutimed Hydro B, BSN Medical, Hamburg, Germany; and Stomahesive base plate, Convatec, Deeside, UK) have allowed patients to continue using their preferred diabetes devices despite the development of ACD [44, 45]. There is currently no consensus on how to treat these patients or how to resolve the emerging problem with these devices, other than to switch to a device that does not contain the culprit allergen, or use more traditional methods for subcutaneous insulin injections in T1DM.

## Limonene and Linalool

Limonene and linalool are natural terpenes found in oils, fruits, trees, grasses, and tobacco [46]. Oxidation of limonene and linalool results in allergenic hydroperoxides that have been increasingly implicated in pediatric ACD [47]. More recently, linalool and limonene have been found to be prevalent in many personal care products and detergents used in children. Linalool has been found in 90% of common essential oils, which are frequently applied directly to the skin or diffused, in which case they may cause an airborne contact dermatitis. Testing of limonene/linalool alone is unreliable in detection of ACD; their hydroperoxides must be included in patch testing to yield pertinent data. Notably, these hydroperoxides are not included in available patch test fragrances mixes and must be tested separately. A recent retrospective review found that these allergens were tested less than half the time in the pediatric population [48]. The review also found that among patients who tested positive to limonene/linalool, more than 50% also tested negative to fragrance mix I/II or balsam of Peru, thus it has been recommended that hydroperoxides of limonene/linalool should be tested in anyone suspected of having fragrance allergy. Limonene/linalool are reported to induce false-positive irritant reactions on patch testing, therefore a delayed reading on day 7 could be considered to attempt to discern a true-positive from an irritant reaction [46–48]. The evolving data on limonene, linalool, and their allergenic hydroperoxides further highlights the importance of understanding the particular and nuanced allergens applicable to our pediatric patients.

## Shin Guard Dermatitis

The 2021 Contact Allergen of the Year is also relevant to the pediatric population. Acetophenone azine is a recently discovered allergen that is generated during the manufacturing process of products made of ethylene vinyl acetate (EVA)-based copolymer foam. There have been multiple case reports of shin dermatitis due to acetophenone azine in soccer shin pads. It is likely that acetophenone azine ACD was the culprit in some cases of shin guard dermatitis previously diagnosed as ICD. In addition, this allergen has been reported in flip flops and other shoes [49].

## Pediatric Patch Testing

Patch testing is the gold standard in the diagnosis and management of ACD in patients of all ages. Conducting patch testing in children presents unique challenges. Please refer to Table 3 for recommendations and special considerations in patch testing in children.

**Table 3** Indications and special considerations for patch testing in children**Indications:**

- Suspected allergic contact dermatitis
- Persistent dermatitis or atypical distribution
- Head/neck
- Hands/feet
- Diaper/perineal
- Shins
- Late childhood or adolescent-onset atopic dermatitis
- Dermatitis that is treatment refractory
- Prior to the initiation of systemic medications

**Special considerations:**

- Particular emphasis on assessment of potential allergens related to sports, hobbies, daycare, school, occupational exposures, and personal care products
- Make patch test panel selection based on relevant exposures from patient/family history:
  - Initial patch test with T.R.U.E. Test or Pediatric Baseline Series
  - Consider custom panel with personal care products
  - Additional expanded panels based on history

Tam and Yu [4], Neale et al. [200, 5000], Sindle et al. [29]

**T.R.U.E. Test**

The thin-layer rapid-use epicutaneous patch test (T.R.U.E. Test, SmartPractice Denmark, Hillerød, Denmark) was first FDA-approved for adults in 1994 and received approval in 2017 for use in children 6–17 years of age after a prospective study of 100 patients showed a low rate of adverse events and demonstrated efficacy based on self-reported improvement following testing [25, 5000]. This test includes 35 allergens and 1 negative control separated into three panels [25]. Limitations of the T.R.U.E. Test are the exclusion of important pediatric contact allergens including cocamidopropyl betaine, propylene glycol, fragrance mix II, and decyl glucoside [25, 51]. Notably, up to 37% of patients could test false-negative on patch testing to MCI/MI with the T.R.U.E. Test due to low concentration of MI in this commercially available patch testing product [5000]. In contrast, the ACDS Core and North American Contact Dermatitis Group (NACDG) series test MCI/MI as well as MI alone at higher concentration, which more often elicits a true PPT, thus reducing false-negative reactions.

A retrospective cohort study of pediatric patients evaluated for ACD using the more inclusive North American 80 Comprehensive Series demonstrated that almost half of the positive reactions were to allergens *not* included in the T.R.U.E. Test [25]. Of the 10 most common allergens with positive reactions in this study, three – CAPB, benzoyl peroxide, and propylene glycol – are not in the T.R.U.E. Test [29]. Especially important is the exclusion of CAPB given its high allergy prevalence – 4% in one study – among patients with atopic dermatitis and its frequent inclusion in personal care products misleadingly labeled as “hypoallergenic” for

children [29, 52]. Zug and colleagues reported data on 883 children patch tested over a 7-year period, and compared allergens detected by the NACDG 65- or 70-series to those on the T.R.U.E. Test. They determined that of all the PPT detected by the NACDG series, 66% of these would have been detected if patients were solely evaluated with the T.R.U.E. Test [26]. Notably, this 66% reflected detection of 13 of the 15 most relevant PPT allergens in children. The authors concluded that the T.R.U.E. Test is a useful screening tool for pediatric ACD; however, clinicians need to be aware of common pediatric allergens that are not present on the T.R.U.E. Test panels, specifically those of higher clinical relevance such as propylene glycol and decyl glucoside [26]. This study also found that 23.6% of children had a PPT to a supplemental allergen that is not part of a standard patch testing series, reinforcing the importance of focused and specialized patch testing if initial testing is negative yet clinical suspicion for ACD remains high [26].

**Pediatric Baseline Series**

In an effort to improve patch testing procedures in children, the Pediatric Baseline Series (PBS) was proposed in 2018 [29, 52]. The PBS is based on survey and workgroup data collected from patch testing professionals and is the first comprehensive pediatric allergen panel in the United States. It is designed for use in children older than 6 years and includes 38 allergens with 2 additional spaces for allergens of the provider’s choice [53]. A study which examined the ability of the PBS and T.R.U.E. Test to diagnose pediatric ACD using PCDR data showed that the PBS was superior to T.R.U.E. Test in identifying PPT [54]. The authors posit

this is due to the inclusion of common pediatric allergens in the PBS including methylisothiazolinone, propylene glycol, cocamidopropyl betaine, propolis, and iodopropynyl butylcarbamate [54].

No commercially available patch test panels carry an FDA indication for children under 6 years old; contact dermatitis experts can choose to use a commercially available patch test or create a customized one, though the latter necessitates greater infrastructure as it requires having a selection of allergens readily available in the patch testing clinic [5•, 52]. Additional, specialized patch test series have been created to evaluate for diaper dermatitis [50••].

In 2016, to reduce and proactively avoid pediatric ACD, the Pre-Emptive Avoidance Strategy (P.E.A.S.) was published. The P.E.A.S. was the result of a study attempting to quantify the effect of avoiding common allergens in personal care products. The authors generated a list of the top 10 allergens based on a systematic review of five studies of patch testing in children. The results suggested that if pediatric patients were to avoid the top 10 most common allergens in personal care products, it would likely prevent 33% of pediatric ACD cases. Hand-outs and cards were created (Table 4) listing products free of these 10 allergens. It was proposed that in conjunction with nickel avoidance and increased nickel surveillance and regulation, this could lead to a significant reduction in pediatric ACD. The P.E.A.S. can be used proactively in those wishing to avoid products with common allergens, or in targeted manner after patch testing has been completed. Despite the simplistic utility of P.E.A.S., it must be stressed that the gold standard in diagnosis, evaluation, and management of ACD is patch testing. Patch testing is the only diagnostic tool that can allow

for definitive diagnosis of ACD, followed by specific avoidance of proven allergens. Patients patch tested by ACDS members may be provided with personalized lists of safe products from the ACDS CAMP database, which is regularly reviewed for accuracy and also includes educational materials prepared by contact dermatitis experts. There are also several online resources for patients to find “safe” products including SkinSAFE ([Skinsafeproducts.com](http://Skinsafeproducts.com)); however, this information must be carefully interpreted by the consumer as it is often created *without* physician consultation [16, 55].

### Practical Points About Pediatric Patch Testing

The smaller surface area of the back in a pediatric patient can make physical application of patches more challenging. One author’s experience is that patients 2 to 4 years of age have space for application of between 40 and 45 allergens, while those 6 years old can accommodate 40–60 allergens [29, 52, 53].

There is limited evidence to suggest a decreased contact time or dilution of allergens for patch testing in children younger than 5–8 years old [5•, 29, 50••]. Our experience is to use standard contact times and concentrations in all of our pediatric patch tests, regardless of age. For children older than 12 years, traditional adult patch testing procedures are routinely recommended [29]. A hypoallergenic tape (Scanpor [SmartPractice], Phoenix, AZ) can be used to secure the patches and they can be reinforced with a stronger medical tape such as Hypafix (Smith and Nephew, Hato Rey, Puerto Rico) for extra security in highly active and mobile children [50••, 52]. Video cartoon distractions are helpful to

**Table 4** Personal care products free of top 10 pediatric contact allergens

Product type	Brand & product
Cleansers	<b>Albolene</b> Moisturizing Cleanser Unscented, <b>Aqua Glycolic</b> Facial Cleanser, <b>Bella</b> Dry Skin Formula Moisturizing Body Bar, <b>CeraVe</b> Hydrating Cleanser, <b>Cleure</b> Glycerin Face/Body SLS Free Soap, Dermalab, Free and Clear, <b>Magick Botanicals</b> Unscented Bar Soap, <b>Neutrogena</b> Ultra Gentle Hydrating Cleanser, <b>Vanicream</b> Gentle Facial Cleanser, <b>VMV</b> Hypoallergenic Moisture Rich Creammy Cleansing Milk for Dry Skin
Moisturizers	<b>CeraVe</b> Moisturizing Cream, <b>Cetaphil</b> Intensive Moisturizing Cream with Shea Butter, <b>Cleure</b> Body Lotion for Dry Sensitive Skin, <b>Derma Topix</b> Intensive Hand Cream, <b>EltaMD</b> Moisturizer Intense, <b>Eucerin</b> Professional Repair Extremely Dry Skin Lotion, <b>Exederm</b> Soothing Baby Oil, <b>Glaxal base</b> Moisturizing Cream; <b>Magick Botanicals</b> Oil Free Moisturize Lotion, <b>Neutrogena</b> Norwegian Formula Hand Cream Fragrance-Free, <b>Theraplex</b> Emollient for Severely Dry Skin, <b>TriCalm</b> Clinical Repair Cream, <b>Cheryl Lee MD</b> Sensitive TrueLipids Relieve and Protect Ointment, <b>Vaniplly</b> Ointment Dry Skin Care for Sensitive Skin, <b>Vaseline</b> Petroleum Jelly, <b>VMV</b> Hypoallergenic Hydra Balance Smart Moisturizer for Combination Skin
Shampoos	<b>AFM</b> SafeChoice Shampoo and Body Wash, <b>VMV</b> Hypoallergenic Essence Skin Saving Clark Wash Hair + Body Big Softie Shampoo and Essence Skin-Saving Superwash Hair + Body Milk Shampoo
Conditioners	<b>Cleure</b> Replenishing Conditioner, <b>DHS</b> Conditioning Rinse with Penthenol, <b>Free &amp; Clear</b> Hair Conditioner for Sensitive Skin, <b>Magick Botanicals</b> Spray on Detangler and Conditioner
Atopic dermatitis medications	<b>A&amp;D</b> EpiCream Skin Barrier Emulsion, <b>Aurstat</b> Anti-Itch Hydrogel, <b>Eleton</b> Cream, <b>Tetrix</b> Cream

Adapted from the P.E.A.S study Hill et al. [11•]



encourage patient cooperation during patch test placement [56].

### Repeat Open Application Testing

Repeat Open Application Testing (R.O.A.T.) is a patch testing adjunct that entails the repeated application of a patient's own personal care product in an attempt to elicit a positive reaction by simulating real-world use [50••, 52]. It can be used if a suspect allergen is not available for patch testing, if the patch test was negative despite high clinical suspicion, or to evaluate the safety of a new personal care product [30, 50••, 52]. R.O.A.T. is performed by applying a suspected allergen twice daily for 7–14 days to the volar forearm [30, 50••, 52]. Rinse-off products should be applied and rinsed off as they would be in daily practice [50••].

### Patch Testing on Immunosuppressants, Phototherapy, and Dupilumab

It is generally accepted that systemic steroids dosed above 10–20 mg per day (in adults) and phototherapy within 1–2 weeks (within 6 weeks with the most conservative recommendations) of patch testing can blunt patch test results [50••, 57]. There is, however, a general lack of literature regarding the use of systemic agents and their effect on patch testing in children [30]. The European Academy of Allergy and Clinical Immunology (EAACI) position paper on patch testing in children acknowledges that little data exist on the effect of immunosuppressants on patch testing results. They recommend avoiding patch testing on immunosuppressives or phototherapy as it could mask weak reactions [58]. If this cannot be avoided, and if allergy is suspected despite negative results, alternative options would be re-testing or performing a delayed reading to capture late reactions [58].

Dupilumab, an injectable IL-4 receptor antagonist, is increasingly being used for the management of chronic dermatitis and recently received FDA approval for atopic dermatitis in children 6 years and above. The question of its effect on patch testing results is now even more salient. There are multiple small case series documenting the use of dupilumab to treat ACD and a clinical trial is actively

recruiting adult patients with ACD who will undergo treatment with dupilumab [59]. One retrospective study evaluated the difference in patch testing results before and after dupilumab initiation [60]. Forty-eight patients with atopic dermatitis were included, with ages ranging from 17 to 92 years, many of whom had a childhood history of atopy [60]. The authors concluded that dupilumab did *not* uniformly weaken patch test results based on the change from definitely positive to definitely negative in only 13/125 patch test pairs [60].

A recent systematic review included 19 studies (72 patients) examining the effects of dupilumab on ACD and patch testing. Dupilumab resulted in clearance of ACD in some patients, partial improvement in a large proportion, and no improvement or worsening in others. Pre- and post-dupilumab patch test results were available in 144 instances: 17 positive patch tests were lost, 8 new reactions developed, and 71 were persistent (48 unknown). The effect of dupilumab on patch testing was variable; the authors posit this may be due to differential immune polarization of allergens [61]. While there is need for further investigation, the data thus far suggest that patch testing results are generally reliable during treatment with dupilumab. In cases of suspected ACD, it would be prudent to perform patch testing prior to starting therapy with dupilumab.

### Limitations and Potential Complications of Patch Testing

Patch testing in children is safe and well tolerated. One rare potential complication of patch testing in patients with atopic dermatitis colonized by *Staphylococcus aureus* is the development of secondary bacterial infection, which was described by Admani et al. in a case series [62]. The authors propose preemptively using aseptic soaks (to be discontinued 4 days prior to patch testing) and avoidance of personal care products containing potential irritants such as cocamidopropyl betaine, fragrance, and formaldehyde to prevent this complication [62]. See Table 5 for further limitations and potential complications of pediatric patch testing.

Active sensitization is a rare adverse event that occurs when a patient undergoing patch testing develops contact

**Table 5** Limitations and potential complications of pediatric patch testing

False-positive irritant reactions
Poor adherence to protocol
Less body surface area for application of patches
Infection
Angry back syndrome (generalized hypersensitivity reaction around sites of applied patches)
Induction of allergy or sensitization through patch testing

Neale et al. [2••, 50••], Admani et al. [62], Chen et al. [65]

allergy to a tested allergen [63]. This reaction is distinguished from a true PPT as it occurs more than 14 days after patch test placement, and can be confirmed with repeat patch testing. To date, there are no documented reports of active sensitization in children from patch testing [63].

“Angry back” or “excited skin” syndrome is a complication of patch testing in which false-positive reactions occur in close proximity to strong true-positives. The precise etiology of angry back syndrome is unclear; however, it may be due to a potent allergen inducing a state of hyperreactivity in the skin, or a preexisting dermatitis that lowers the threshold for cutaneous irritability. These false-positive reactions are not reproducible on subsequent patch testing, and can cause considerable confusion for patients who may be labeled as “multiple reactors” or are simply diagnosed with a flare of their underlying skin disease [64]. There is extremely limited data on “angry back syndrome” in children, though in general, children with extensive flaring of their dermatitis should defer patch testing until the flare has improved [65].

One major limitation to patch testing has always been a lack of providers qualified to administer the test and interpret its results. This is exemplified by the dearth of providers willing to perform pediatric patch testing, which is likely at least in part due to the now debunked fears regarding safety of patch testing in children [25, 63, 66, 67].

### Patch Testing and Telehealth

The medical community has experienced a rapid expansion of telehealth in large part due to the COVID-19 pandemic. Even prior to the pandemic, however, a group of experts advocated for the development of a direct-to-consumer telehealth platform specifically for ACD [68].

A recent report described virtual patch testing performed for 10 patients during the COVID-19 pandemic [69]. Due to restrictions imposed by the government of New Zealand, these patients had a final patch test reading via telehealth [69]. Digital photography was used and the author specifically noted the use of “oblique photographs of individual patches” to help discern induration from epidermal change. Although the results were imperfect, this series provided evidence that virtual patch test reading can be considered, which would allow greater access to rural communities and patients/families without reliable transportation [69]. A more recent study compared the interpretation of patch test results between in-person evaluation and tele-dermatology evaluation. The outcomes included agreement in patch test results, reading interpretation, and final assessment (allergic, indeterminate, irritant, negative). Ultimately in-person

and tele-dermatologists *completely* disagreed in the interpretation of patch test results for over 13% of patches at the second reading, and almost 25% for the final assessment. Failure did correlate with lower perceived quality of images, suggesting that one limitation of tele-dermatology for patch testing is the quality or resolution of the images provided [70]. There is a paucity of data regarding pediatric-specific virtual patch testing, with a single report in the English-language literature of a 15-year-old girl whose final assessment was performed via tele-dermatology [69]. We argue that further analyses of the utility of virtual patch testing should aim to include pediatric patients. The assessment of these cases is unique in that it would need to be done by a parent or caregiver and a cooperative child, which may add a further layer of complexity to the success of virtual patch testing.

### Conclusion

This article seeks to address common misconceptions, challenges, and concerns regarding ACD in the pediatric population, while emphasizing the important role patch testing plays in its evaluation and management. Despite previous misconceptions, it is now recognized that ACD is not uncommon among children. Chronic, refractory, or atypical dermatitis in the pediatric patient warrants evaluation with appropriately targeted patch testing. Patch testing is safe and effective when the performing provider takes into consideration the nuances of such testing in a young patient, as well as the limitations of commercially available patch tests. There are continuously new and evolving contact allergens, as evidenced by the “unmasking” of allergens during the COVID-19 pandemic, and the advancement of technology leading to new avenues of allergen exposure, such as diabetes devices. The management of pediatric contact dermatitis requires a thorough evaluation, appreciation of patient-specific factors, and a measure of patience, which, when taken together, can lead to a satisfactory and treatment-altering diagnosis.

### Compliance with Ethical Standards

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