# Pediatric allergic contact dermatitis. Part 2: Patch testing series, procedure, and unique scenarios



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#### Learning objectives

After completing this learning activity, participants should be able to explain the methods and challenges of patch test evaluation in children; describe the baseline series available for use in children and the evidence supporting its use; identify the most relevant allergens to test in children of various ages and location affected; explain unique patch testing scenarios in children and its evidence for use including food and drug hypersensitivity patch testing; and discuss treatment methods and empiric allergen avoidance strategies in children.

#### Disclosures

#### Editors

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Patch testing is the criterion standard for diagnosing allergic contact dermatitis. Causative allergens differ between children and adults, necessitating the development of pediatric-specific patch test series. The Pediatric Baseline Series was developed in 2018 through expert consensus and includes relevant pediatric allergens that dermatologists can use in practice. Obstacles in patch testing, such as the need for multiple office visits, length of patch application, and avoidance of sweat and water on the testing area, are particularly challenging for the pediatric population, and several strategies are proposed. Aside from formal patch testing, alternatives like the repeat open application test and empiric allergen avoidance can be helpful in children. The key to management of allergic contact dermatitis is allergen avoidance, with emphasis on the need to properly identify causative allergens. Continued data collection through registries allows for a better understanding of the diagnosis and management of pediatric allergic contact dermatitis. (J Am Acad Dermatol 2021;84:247-55.)

*Key words:* ACD; allergens; patch testing; pediatric ACD; pediatric allergic contact dermatitis; Pediatric Baseline Series.

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#### Abbreviations used:

ACD: allergic contact dermatitis

ACDS: American Contact Dermatitis Society

APT: atopy patch test

FDA: US Food and Drug Administration

IR: irritant reaction
 MI: methylisothiazolinone
 PBS: Pediatric Baseline Series
 PEAS: pre-emptive avoidance strategy
 ROAT: repeat open application test
 TRUE: Thin-Layer Rapid-Use Epicutaneous

Part 1 of this continuing medical education article discussed underrecognition and testing of pediatric allergic contact dermatitis (ACD). Patch testing, first formally described more than a century ago, <sup>1</sup> is key for the accurate diagnosis and management of ACD, ultimately leading to improved quality of life in those tested.<sup>2</sup> It is thus important for children who are suspected of having ACD to be patch tested. Part 2 of this continuing medical education describes pediatric-specific patch series, discusses practical methods of patch testing and allergen alternatives, and provides management strategies for pediatric ACD.

# PATCH TESTING SERIES FOR CHILDREN Key points

- Having a consensus on the allergens to patch test in children is a key step in overcoming a major challenge in diagnosing allergic contact dermatitis in children
- The first US expert-derived, pediatric-specific patch test series was developed in 2018, called the Pediatric Baseline Series

Until recently, there has been little guidance for providers in selecting the appropriate patch series for children. Physician-reported barriers to pediatric patch testing include a lack of series approved by the US Food and Drug Administration (FDA) in addition to the absence of consensus on allergens to test.<sup>3</sup> In 2017, the FDA approved the Thin-Layer Rapid-Use Epicutaneous (TRUE) test (Smart Practice) to diagnose ACD in children 6 to 17 years old. However, the inability to customize allergens based on exposure history limits the clinical utility and diagnostic accuracy of this test. Furthermore, it does not include several common pediatric allergens, such as propylene glycol, cocamidopropyl betaine, and fragrance mix II. Additionally, although the TRUE test includes methylisothiazolinone (MI) as a component of a 3:1 mixture (methylchloroisothiazolinone/MI), the concentration of MI is often too low to detect stand-alone

MI allergy.<sup>5</sup> Therefore, using the TRUE test alone can result in missing more than half of positive reactions in children.<sup>6</sup>

Comprehensive panels such as the American Contact Dermatitis Society (ACDS) Core 80 Series and North American Contact Dermatitis Group Series have been used in older children; however, these are not always practical for younger children, because space is limited on the back of a young child. Most existing panels were derived and updated based on epidemiologic data in adults, but it is known that children and adults have different sensitization profiles (see Part 1).

To address these limitations, members of the ACDS created the first collaborative and comprehensive expert-derived pediatric panel (Pediatric Baseline Series [PBS]) (Table 1). The PBS is a reference point to be built on with patient-specific relevant allergens, permitting customization based on a patient's exposure, personal products, and distribution of dermatitis as well as provider experience. Adding supplemental allergens is meaningful in patch testing because more than 20% of children had a positive reaction to products outside of standard screening panels. 9

There are regionally specific baseline series as well, including Australia's baseline series for children containing 30 allergens<sup>10</sup> and the European Academy of Allergy and Clinical Immunology baseline of 9 allergens (with 12 supplemental allergens for use according to history). <sup>11</sup> Specific patch series also exist for diaper dermatitis, <sup>12</sup> metal implants in children, <sup>13</sup> and sunscreen ingredients. <sup>14</sup>

### **PATCH TESTING PROCESS**

#### **Key points**

- Proper patch testing technique will maximize reproducibility and accuracy
- A key step in patch test interpretation is a thorough history to determine relevance

#### **Procedure**

Patch testing is a time-intensive process. The child will attend a minimum of 3 office visits over 1 week (Fig 1). The initial visit includes a thorough history and physical examination. Patches may be placed during the first visit to minimize additional visits. Patients are advised against getting the back wet for optimal results and are thus discouraged from showering and strenuous physical exercise that may induce sweating. Itching and rubbing of the back are also discouraged because they may lead to patch displacement. After 48 hours (24 hours for children younger than 8 years to prevent irritant

**Table I.** Allergens in the pediatric baseline series<sup>7</sup>

<u> </u>		
Allergen		
Nickel sulfate	Carba mix	
Quarternium-15	lmidazolidinyl urea	
Neomycin	Amerchol-L101	
Balsam of Peru	Compositae mix	
Fragrance mix I	Cinnamic aldehyde	
Methylchloroisothiazolinone/ methylisothiazolinone	Paraben mix	
Bacitracin	Thiuram mix	
Propylene glycol	Bronopol	
Methylisothiazolinone	Sesquiterpene lactone	
Fragrance mix II	Colophony	
Cocamidopropyl betaine	p-tert-Butylphenol formaldehyde resin	
Cobalt chloride	Clobetasol-17-propionate	
Formaldehyde	Decyl glucoside	
Propolis	lodopropynyl butylcarbamate	
Tixcortol-21 pivalate	Benzophenone-3	
Hydrocortisone-17-butyrate	Amidoamine	
Diazolidinyl urea	Tea tree oil	
1,3-dimethylol-5,5- dimethylhydantoin	Carmine	
Budesonide	Dimethylaminopropylamine	

reaction [IR]),<sup>6,15</sup> the patches are removed, and reactions are recorded and marked. After removal, the patient may carefully bathe and partake in gentle physical activity to prevent erasing the patch markings. The child then returns to the clinic again 48 hours after removal for the final reading. <sup>16</sup> The final reading timeframe varies depending on patch testing experts (24-120 hours after removal). Literature reports suggest that a final reading more than 48 hours after removal can miss important allergens, including fragrances and preservatives, which are among the most common allergens in children. <sup>16-18</sup>

Allergens for patch testing are available for purchase from Dormer Laboratories, SmartPractice, or SmartPractice Canada. <sup>19-21</sup> The allergens are supplied in either a petrolatum base in a syringe or aqueous solution in a dropper bottle. Approximately  $20~\mu l$  of a petrolatum-based allergen or 1 drop (approximately  $15~\mu l$ ) of a liquid-based allergen is dispensed into patch testing chambers, which include Finn Chambers (SmartPractice), allergEAZE Chambers (SmartPractice), and IQ Ultra/Ultimate chambers (Dormer). <sup>22-24</sup> Patches are placed on the child's back, avoiding the spine, and reinforced with hypoallergenic tape (eg, Scanpor [SmartPractice]) (Fig 2).

Personal products can also be patch tested. Products that are intended to be left on the skin (moisturizers, sunscreen, makeup) can be directly applied to a patch chamber and tested as is. Wearable materials (clothing, watch bands, sports equipment, shoes) can be directly applied to the skin after wetting with water or saline to mimic sweat.<sup>25</sup> If there is no reaction noted at the time of patch testing removal, the substance should be reapplied after rewetting and remain in contact with the skin until the final reading.<sup>26</sup> Products that are meant to be washed off (soap, shampoos, conditioner) should be diluted according to recommendations by de Groot<sup>27</sup> because of the risk of IR; however, dilution comes with the risk of false negatives and does not guarantee prevention of IRs, and thus, results should be interpreted with caution. Unknown substances, detergents, industrial oils, or anything that is not intended to be in contact with the skin (cleaning agents, pesticides, etc) should absolutely not be tested.

## Interpretation

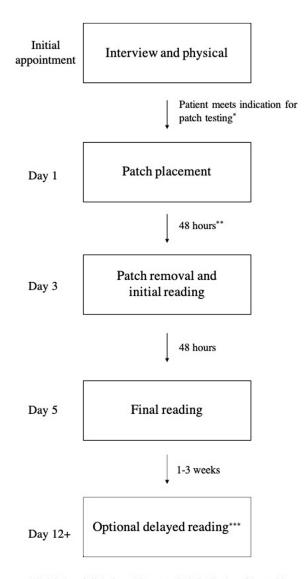
Patch test reading is usually performed on the day of patch test removal (24 or 48 hours depending on age) and optimally at 48 hours after removal. An optional delayed reading can be performed 1 to 3 weeks after patch application, because some allergens (eg, neomycin, corticosteroids, metals, preservatives) can cause delayed reactions. A crescendo reaction between the initial reading and the final reading suggests a positive reaction. A decrescendo reaction between the 2 readings is suggestive of an IR.

A positive patch test will show erythema, papules, vesicles, or bullae depending on the severity of the reaction, which may be graded according to the International Contact Dermatitis Research Group recommendations (Table II). 30,31 Importantly, the strength of a reaction is not equivalent to clinical relevance. Establishing the relevance of a positive reaction as the cause of ACD is the most important step in patch testing. It is determined through history, review of product ingredients, and exposure (including contacting manufacturers when product ingredients are unavailable). Although stronger reactions have a higher likelihood of being reproducible, 32 strength of reaction does not always hold meaningful bearing. For example, a strong reaction to an allergen with no known exposure history is not more relevant than a weak reaction in a patient with an exposure history connected to a product containing that allergen.

# OBSTACLES, RISKS, AND POOR CANDIDATES

## **Key points**

• There are various techniques to help ease the process of patch testing in children



\*High index of clinical suspicious; atypical distribution of dermatitis; recalcitrant/therapy resistant dermatitis

Fig 1. Pediatric allergic contact dermatitis patch testing: typical office visit timeline.

 Patch testing is a low-risk diagnostic procedure, and adverse effects, including active sensitization, have not been reported in children

Although pediatric patch testing can be challenging, strategies can be implemented to ease the process (Table III).

IRs to patch testing are challenging because they are often mistaken for positive reactions. Children may be at increased risk for IR because of inherent qualities of younger skin (eg, faster stratum corneum turnover and increased circulation), which is thought to lead to both a stronger inflammatory response and increased cutaneous absorption of irritants in

younger children.<sup>33</sup> However, a multicenter pediatric ACD study did not show any significant difference of IRs to individual allergens between children and adults.<sup>34</sup> IRs in pediatric patch testing are most likely to be reported from metals, preservatives, cocamidopropyl betaine, and fragrances.<sup>34</sup> Avoiding IRs is particularly challenging because strategies that decrease irritancy come at the expense of potentially missed positive ACD responses. For irritancy avoidance, it is acceptable for children younger than 8 years to leave allergens on for 24 hours instead of the standard 48 hours used in adults and older children. 15,35,36 A less common strategy that can be used in infants for IR avoidance is to halve the concentrations of irritating allergens (such as metals), 11 although the potential for false negative results should be noted with this method. Children older than 6 years can be safely tested with the concentrations used in adults.<sup>37</sup>

Between child and caregiver schedules and responsibilities, 3 office visits can be difficult to manage. If multiple visits are not possible, parents may remove patches at home under the guidance of the clinic. Markers should be provided to carefully mark the area to allow interpretation during the final reading. If returning to the office for the recommended reading schedule (days 3 and 5) is not possible, working with the family to determine alternative reading times may be offered at the expense of test accuracy. 38 Single readings 72 to 96 hours after patch application (day 3 or 4) may be performed in limited circumstances, although they come with the risk of missing at least 5% to 17% of positive reactions. 38,39 Home patch tests have not been tested in children and are not the standard of care. Recent experiences show poor interpretability of photographs taken by patients of final patch testing results. 40,41

Cooperation may pose patch testing challenges in children. Patch placement takes approximately 15 to 30 minutes, during which time a child may feel restless or anxious. Video distraction, 42 assurance that needles will not be used, taking patches home for mock application, and risk/reward are reported to be successful strategies.<sup>35</sup> Additional difficulties include avoiding sports and the inability to wet the back during bathing/showering after patch placement. Working with families to determine the most convenient time for patch testing can overcome this obstacle, such as during the off-season for sports. Once patches are physically removed, patients may choose to return to bathing and physical activity, albeit cautiously, so long as they are able to re-mark the patches.

The size of a child's body may limit space for patches. It is estimated that the back of an average

<sup>\*\*24</sup> hours for children under 8 years

<sup>\*\*\*</sup>Neomycin, methylchloroisothiazolinone/methylisothiazolinone, and corticosteroid allergy may show delayed reactions

**Fig 2.** Pediatric allergic contact dermatitis patch test placement. **A**, A total of 80 patches can fit snugly on a 7-year-old. **B**, Patches are reinforced with Scanpor tape (SmartPractice).

**Table II.** International Contact Dermatology Research Group patch test interpretation<sup>31</sup>

• •	•	
Morphology	Interpretation	Symbol
No reaction	Negative	-
Faint erythema only	Doubtful	+/-
Erythema, infiltration, and possible papules	Weak positive	+
Erythema, infiltration, papules, and possible vesicles	Strong positive	++
Intense erythema, infiltration, and coalescing vesicles or bullae	Extreme positive	+++
Irritant morphologies (xerotic, roughness, glazed appearing, or fissuring)	Irritant	IR

6-year-old holds 40 to 60 allergens.<sup>7,35</sup> To overcome this, the PBS (38 allergens) can be used as a baseline series for children, patches can be placed on the abdomen or thighs,<sup>25</sup> or serial testing starting with most suspected allergens can be performed.

#### Risks

The process of patch testing is safe and well-tolerated. There is the rare risk of sensitization through exposing the child to new allergens. Studies on adults show that these reactions occur more than 1 week after the application of patches in less than 1% of patients, <sup>43</sup> although no cases of active sensitization in children have been reported.

Patch testing can result in a false negative test result if the allergen concentration is too low, if the chambers have inadequately adhered through

**Table III.** Strategies for overcoming challenges in pediatric patch testing

Challenge	Strategy
Irritant reaction	Halve concentrations of allergens*
	Limit time of allergen occlusion to 24 h <sup>†</sup>
	Follow up with repeat open application test
Lack of	Use of video distraction <sup>42</sup>
procedural	"No needle" assurance <sup>35</sup>
cooperation	"Risk and reward" psychology <sup>35</sup>
·	Patch samples for at-home mock application
Limited space for	Use of thighs and then abdomen for patches
patches	Use of smaller, pediatric-specific patch series
	Serial patch testing with highest-yield allergens first
Difficulty returning	Single patch test reading on day 3 or 4 <sup>39,*</sup>
to office for readings	Removal of patches at home by parents Request patient photographs for delayed readings

<sup>\*</sup>May increase likelihood of false negative result.

improper placement or dislodgement, or if the culprit allergen was not tested. False negative test results can complicate the management of ACD, because the diagnosis remains indeterminate, and the patient leaves not knowing what to avoid. This may lead to prolonged suffering, exposure to topical and systemic immunosuppressants, and costly investigation of alternate diagnoses.

<sup>&</sup>lt;sup>†</sup>Typically performed for children younger than 8 years.

## Special considerations

Children with extensive dermatitis involving the back should not be patch tested because of the risk of a false positive flare and the development of angry back syndrome. Angry back syndrome is the development of cutaneous inflammation that cannot be reproduced when allergens are tested separately. A4,45 These children should return for patch testing when the back is sufficiently clear to place patches. Strategies to clear the back include soaking and smearing with topical steroids and/or bland emollients, oral prednisone, or cyclosporine that is tapered to the lowest possible dose before patch testing.

To avoid false negative reactions, it is recommended that topical steroids to the back be avoided at least 3 to 7 days before patch testing. 47,48 Additionally, those with a suntan, burn, or excessive ultraviolet exposure to the back should wait 6 weeks before patch testing (if possible) because of the immunosuppressive effect of such exposure to the skin. 49,50

False negative patch test results may occur while taking systemic immunosuppressants. A randomized controlled trial of adults indicated that oral prednisone (20 mg daily) suppressed patch test reactions.<sup>51</sup> However, studies have shown that positive patch test results can still be elicited while on immunosuppressive agents. Reports of patients with positive patch reactions while taking immunosuppressants and tumor necrosis factor  $\alpha$  inhibitors exist.<sup>52</sup> It is likely that strong reactions remain positive, albeit weaker, while on these agents, but weak positive reactions may be suppressed. High clinical suspicion should be maintained while performing a final reading, and repeat testing should be performed if clinical suspicion of ACD remains but the patch testing result was negative. If possible, such systemic agents should be tapered or discontinued before patch testing depending on half-life and dosage.<sup>11</sup>

Dupilumab, FDA approved for atopic dermatitis in children 6 years and older, is not a contraindication for patch testing. A recent study suggested that patch test results were unlikely to be dampened in children on dupilumab in the majority of cases. <sup>53</sup> Thus, patients who meet patch testing indications may be tested while continuing this medication.

# **UNIQUE PATCH TESTING SCENARIOS Key points**

 Repeat open application testing and empiric allergen avoidance are 2 different strategies that can be used in children who cannot undergo patch testing or in cases of suspected false negative patch test reactions  Atopy patch testing may be used to diagnose some food or aeroallergen allergies in select children, although utility is controversial

### Repeat open application testing

A repeat open application test (ROAT) involves applying a suspected product to a 2.5-cm area on the non—sun-exposed volar forearm twice daily for up to 2 weeks to determine if the patient has ACD to the product. Froducts that are meant to be left on the skin (moisturizing creams) can be applied as is to the skin. Rinse-off products such as soaps should be applied and then washed off, reflecting daily use. Products that are not intended to be applied to the skin (such as detergents and unknown chemicals) should never be tested on the skin by any method because of the risk of irritation and caustic injuries.

ROAT can confirm a weak or suspected false negative patch test result and, if no reaction is seen, can determine if a new product is safe to use. ROAT has also been used in clinical testing to determine the tolerability of developing pediatric products. <sup>55</sup>

### Empiric allergen avoidance

Children who are unable to be patch tested or have negative patch test findings with a remaining high clinical suspicion may benefit from the preemptive avoidance strategy (PEAS). In PEAS, the top pediatric allergens are avoided, and a safe product list is given. It is estimated that one third of children with ACD may have benefited from this strategy. FEAS, initially developed based on 10 allergens, has now expanded to include 25 common pediatric allergens (Table IV). To

## Food and drug hypersensitivity patch testing

Atopy patch tests (APTs) use protein allergens such as those found in aeroallergens and foods (eg, egg, milk) under occlusion, similar to traditional patch testing, to elicit a delayed immunologic response. Although some studies report that APTs are specific and sensitive in diagnosing food allergies, 59,60 many researchers do not support standalone APTs, and their utility is controversial. 61

# PRINCIPLES OF MANAGEMENT Key point

The first-line treatment of allergic contact dermatitis is allergen avoidance, education, and finding safe products that do not contain culprit allergens

#### Detection, avoidance, and education

Patch testing is the most important step in the diagnosis and management of pediatric ACD. The primary treatment for ACD is avoidance of allergens. Most patients who avoid a known allergen

Table IV. Personal care product allergens to avoid in the pre-emptive avoidance strategy<sup>57</sup>

	p		
Product category	Recommended allergens to avoid in the pre-emptive avoidance strategy		
Fragrances	Components of fragrance mix I and I		
	Balsam of Peru		
	Cinnamic aldehyde		
Preservatives	Methylchloroisothiazolinone/		
	methylisothiazolinone		
	Methylisothiazolinone		
	Formaldehyde		
	Quarternium-15		
	lodopropynyl butylcarbamate		
	Methyldibromoglutaronitrile/		
	phenoxyethanol		
	Diazolidinyl urea		
Antimicrobials	Neomycin sulfate		
	Bacitracin		
	Bronopol		
Emollients	Wool alcohols		
	Propylene glycol		
	Amerchol-L101-lanolin		
Natural additives	Propolis		
	Compositae mix		
	Cocamidopropyl betaine		
	Colophony		
Surfactants	Decyl glucoside		
	Sorbitan sesquioleate		
Corticosteroids	Tixocortol-21-pivalate		
Hair dye/henna tattoo	<i>p</i> -Phenylenediamine		

show improvement of their dermatitis, 62 with studies showing 90% of patients having complete remission.<sup>63</sup> However, avoidance can be difficult without proper guidance. Up to one third of patients do not remember the outcome of their patch test, <sup>64</sup> and the ability to recall allergens has been negatively correlated to both number of allergens and to years after patch testing.<sup>65</sup> Everyone involved with the child should be made aware of known allergens. In addition to avoidance, the treatment of acute inflammation may include cold compresses, topical corticosteroids, phototherapy, or systemic immunosuppressants. 60

#### Safe products for children

Finding safe products may be difficult for patients.<sup>67</sup> Labels on products may be misleading because detergents and sunscreens labeled as "free and gentle," "baby-safe," "sensitive," or "for children" contain common allergens. 68,69 Unscented products may contain masking fragrances. The ACDS has created a Contact Allergy Management Program to help patients and providers find safe

products. The program sorts through a database and identifies safe products in each category such as shampoos, conditioners, soaps, moisturizers, sunscreens, and so on based on the patient's allergens. 70 A similar program, SkinSAFE (HER Inc), is also available for patients and providers to explore safe products based on patch testing results.<sup>7</sup>

## **Pediatric ACD registry**

In 2017, a multicenter pediatric ACD registry was established with the support of the Dermatology Foundation. The goal of the registry is to track the changing prevalence of pediatric ACD. Data published from the registry will inform clinicians and researchers on current trends in pediatric ACD because exposures are constantly shifting, allowing current pediatric patch test series to be updated accordingly.<sup>72</sup>

#### **CONCLUSION**

Although the incidence of ACD is similar in both adults and children, children are patch tested at a lower frequency, and thus, many cases of pediatric ACD are missed. Patch testing is the key to significantly improving the quality of life for the child and their parents. The information gained through patch testing can lead to policy changes such as implementation of nickel-limiting directives 73,74 and restrictions on common allergens, similar to initiatives enacted in Europe. These data can also affect the cosmetic and personal care industries to switch to alternative ingredients. Such changes can have a significant impact on the rates of ACD in both adults and children.

## **Conflicts of interest**

None disclosed.

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## **Answers to CME examination**

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