

Contact Dermatitis in Pediatrics

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ABSTRACT

Contact dermatitis is an umbrella term that describes the skin's reaction to contacted noxious or allergenic substances. The two main categories of contact dermatitis are irritant type and allergic type. This review discusses the signs, symptoms, causes, and complications of contact dermatitis. It addresses the testing, treatment, and prevention of contact dermatitis. Proper management of contact dermatitis includes avoidance measures for susceptible children. Implementation of a nickel directive (regulating the use of nickel in jewelry and other products that come into contact with the skin) could further reduce exposure to the most common allergens in the pediatric population. [*Pediatr Ann.* 2016;45(8):e287-e292.]

Dermatitis is a category of eczematous skin disease that clinically presents as a pruritic, red rash that can be accompanied by vesicles, scaling and, particularly in chronic cases, lichenification. Histologically, dermatitis demonstrates epidermal “spongiosis” (intercellular edema). Contact dermatitis accounts for a large number of pediatric cases of dermatitis. Contact dermatitis is characterized into 1 of 2 main subtypes: allergic or irritant. Allergic contact dermatitis (ACD) represents an acquired sensitivity to an al-

lergen that is a cell-mediated (type IV) hypersensitivity response. Irritant contact dermatitis, on the other hand, manifests as a general inflammatory reaction to a substance that requires no specific antigen-primed immune response.

IRRITANT CONTACT DERMATITIS

Irritant contact dermatitis is the most common type of contact dermatitis in pediatric patients. Common causes of this in children include irritants such as saliva, urine and/or feces, personal care products, cleaning products, diapers, toi-

let seats, certain insects, and sanitizers. Diaper dermatitis is the most common skin disorder in infants and results from excess moisture, friction, urea, and stool enzymes that function to break down the skin's natural barriers and cause irritation.¹ Pediatricians should also be aware that toilet seat dermatitis in children presents in a bilaterally symmetrical distribution on the posterior thighs and buttocks, related to irritation from commercial toilet-cleaning products.² Another cause of irritant dermatitis in the pediatric population is topical envenomation from caterpillars. Finally, as in any age group, excessive hand washing and exposure to harsh soaps or sanitizing solutions can result in irritant hand dermatitis.

ALLERGIC CONTACT DERMATITIS

In the 8 decades that have passed since Dr. Henry Straus' pivotal discovery that neonatal skin could be primed to mount a delayed-type hypersensitivity reaction, the recognition of ACD in children has increased dramatically, with the current prevalence in the general pediatric population estimated to be as high as 24%.³ However, the condition is still underrecognized. In 2015, Jacob et al.^{4,5} and Brod et al.⁶ published a review of flexural dermatitis emphasizing the importance of patch testing to rule out an ACD instigator, particularly in cases of chronic eczema;⁴ however, despite the safety, efficacy, and utility of patch testing, many children are unlikely to be tested.^{5,6} Confounding the diagnosis of ACD in the pediatric population are challenges with provider education, patient

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access to dermatology specialists, and lack of a US Food and Drug Administration (FDA)-indicated patch-test tool for pediatric use.

The etiology of ACD includes an extensive list of potential offenders. General categories include plants, metals, medications, personal care products, body adornments (eg, black henna tattoos), and photoallergic substances. **Table 1** lists common allergens and sources in the pediatric population.^{6,7}

Plants

Within the *Rhus* or *Toxicodendron* genus, there are multiple species associated with contact dermatitis—including poison ivy, poison oak, and poison sumac. Urushiol is the allergen in these plants, and it is found within the sap and comprised of mixed catechols. Common foods such as mangos, pistachios, and cashew nuts contain haptens that can cross-react with *Toxicodendron* plants. The rind of mango, which has the highest concentration of resorcinol, has been implicated in many cases of ACD, with fewer cases reported from contact with the flesh.⁸

The Asteraceae plant family is another well-known cause of ACD. Members of this family include chicory, chrysanthemum, endive, daisy, sunflower, sagebrush, dandelion, lettuce, echinacea, and ragweed. The allergens in this family of plants are sesquiterpene lactones (SLs). SLs are found in the leaves, stems, and flowers of Asteraceae plants. However, a recent study suggests that SLs may also be present in seeds, making it reasonable to caution patients with significant Asteraceae allergy to consider avoiding sunflower seeds and chamomile tea.

Metals

Children in the US are found to be sensitized to nickel most commonly (noting that toxicodendron, a major cul-

prit, is not part of routine testing). ACD caused by nickel can dramatically affect quality of life. On a global scale, this problem is responsible for astonishing health care costs. In the US alone, it is estimated that the combined indirect and direct costs may be as high as \$5.7 billion per year.⁵ Sensitization to nickel can occur in children in numerous ways—jewelry, clothing snaps, coins, toys, electronics, razors, and belt buckles have all been implicated.^{5,9} Piercing the skin and keeping the wound in sustained, direct exposure to nickel is known to increase risk for sensitization. A Finnish study suggests that piercing may increase nickel sensitization rate by 3-fold.¹⁰

Cobalt is the second most common metal cause of ACD. Sources of cobalt can include jewelry, cosmetics, cement, dental/orthopedic implants, blue tattoo ink, and leather dye.

Medications

It is estimated that approximately 10% of the population develops ACD to neomycin, one of the main ingredients in popular, over-the-counter, triple-antibiotic products.¹¹ Neomycin is an aminoglycoside-antibiotic that cross-reacts with other members of the same class (eg, gentamicin and tobramycin). It has been found to coreact with bacitracin in patients who are polysensitized to the two substances due to them having one common source in triple-antibiotic products. Notably, bacitracin is chemically distinct from neomycin and functions by inhibiting cell wall synthesis. Estimated prevalence of bacitracin sensitivity ranges from 1.5% to 9.1%.¹¹

The first case report of corticosteroid allergy was published in 1959, 9 years after the introduction of topical corticosteroids.¹² It has been estimated that corticosteroid sensitivity is as high as 4%, specifically to tixocortol-21-pivalate,

which is the routine testing substance for over-the-counter hydrocortisone.¹³ Topical steroids that are in a halogenated-methylated group, which includes clocortolone and desoximethasone, are considered the least allergenic. It is important to consider testing for a steroid allergy or switching to a different product in cases of clinically diagnosed eczema that either worsen or do not improve with standard topical steroid treatments.

Personal Care Products

Balsam of Peru (also known as *Myroxylon pereirae*, black balsam, or china oil) is a derivative of tree sap from the *Myroxylon pereirae* tree, which is native to El Salvador. It is found in many products, including diaper balms, wound ointments, liquid adhesives, mouthwash, and toothpaste. In patients with severe, systemic allergy to balsam of Peru, it may be beneficial to avoid foods that contain balsam derivatives and/or cross-reacting substances; these include tomatoes, cinnamon, chocolate, cloves, citrus peel, and vanilla extract.

Formaldehyde and formaldehyde-releasing preservatives are found in both personal care and cleaning products, including cosmetics, burn remedies, waxes, polishes, latex paint, and wrinkle-free clothing. Of note, in patients with ACD, this allergen may be irritating, further complicating the interpretation of patch testing. For these reasons, simultaneous product patch testing with the personal care products and topical medicaments (sources) in common use by the patient is recommended.

The first synthetic detergent for household use was marketed in 1933, opening the doors for further developments of synthetic detergents. In 1967, the first patent was granted for the synthetic cocamidopropyl betaine (CAPB) detergent-based, non-tear-inducing shampoo for babies. CAPB is a surfac-

tant often found in shampoos, bath products, and other cleansers. ACD from CAPB, therefore, can present as eyelid, facial, scalp, neck, and/or diffuse dermatitis.¹⁴ Notably, CAPB is not one of the allergens included on the commercially available patch test device.

Tattoos and (Adulterated Black)

Henna

Traditional tattoos can incite ACD, depending on the color and the metal elements used in the tattoo ink. Cobalt (discussed above) is in some blue tattoo ink. Potassium dichromate, another allergenic metal, is found in green tattoo ink.

Natural henna is a dye traditionally used in Hindu culture for body art. The dye comes from the fruit-bearing plant, *Lawsonia inermis*, a large shrub that grows in warm climates. Henna adulterated with the hair dye chemical para-phenylenediamine (PPD) (known as “black henna”) has, unfortunately, gained popularity because it reduces drying time and increases the longevity of the tattoos. PPD concentration in black henna can be as high as 64% compared to only 6% in hair dye, and this puts the exposed consumer at significant sensitization risk. PPD is 1 of 5 chemicals labeled as “strong sensitizers” by the Consumer Product Safety Commission.¹⁵ In 2001, in the wake of increased allergic reactions to PPD, the FDA launched an informational website and hotline where consumers could call in to report adverse reactions to PPD from black henna or other sources. Further, in 2008, the American Contact Dermatitis Society (ACDS) and the American Academy of Dermatology (AAD) joined together to advise a ban on PPD-enhanced henna.¹⁶ Despite these significant efforts, the use of adulterated black henna persists worldwide.¹⁷

TABLE 1.

Commonly Sensitized Allergens and Sources in the Pediatric Population

Allergen	Source
Bacitracin	Topical antibiotic
Budesonide	Corticosteroid (triamcinolone group)
Carba mix	Rubber accelerator
Cobalt chloride	Metal (often allow with nickel)
Cocamidopropyl betaine	Shampoos, cleaners
Colophonium (colophony)	Fragrance/adhesive
Compositae mix/dandelion extract	Ragweed family plant
Disperse dyes (blue 124/106, yellow 3/9)	Aniline dye
Formaldehyde	Preservative
Lanolin alcohol	Emollient
Methylchloroisothiazolinone/methylisothiazolinone	Preservative
<i>Myroxylon pereirae</i> (balsam of Peru)	Fragrance/flavorant; tomato products cross-react with it
Neomycin sulfate	Topical antibiotic
Nickel sulfate	Metal alloys (also naturally in some foods including chocolate)
Potassium dichromate	Metal derived from chromium
Propylene glycol	Preservative, solvent/moistening agent
Quaternium 15	Preservative/ formaldehyde releaser
Tixocortol-21-pivalate	Corticosteroid (hydrocortisone group)

Adapted from Brod et al.⁶ and Jacob et al.⁷

Photoallergic Substances

When certain chemicals applied to the skin or taken orally lead to a subsequent delayed-type hypersensitivity dermatitis after sun exposure, these are considered photoallergic substances. Sunscreens are a common culprit in photocontact dermatitis, particularly those containing oxybenzone or cinnamates.

Although a comprehensive review on systemic contact dermatitis is beyond the scope of this article, it would be remiss not to mention that photoallergic reactions secondary to oral medications are an important category. These type IV hypersensitivities are clinically similar to ACD, with the timing of onset varying

from days to weeks, and the rash typically restricted to sun-exposed areas of the skin.

DIAGNOSIS AND TESTING

In cases of both irritant and allergic contact dermatitis, diagnosis requires a thorough clinical history that extracts a temporal association (**Figure 1**). Removing the suspected offending agent is a test that also can provide treatment if there is symptom relief. In situations where avoidance is not practical, therapy is more challenging (and this is addressed later in this article).

Patch testing (**Figure 2** and **Figure 3**) is the gold standard to diagnose ACD.¹⁸



Figure 1. Fragrance-associated eyelid dermatitis.



Figure 2. Patch testing application.

Notably, to date, the FDA has not approved pediatric use of any of the available patch testing kits that are currently on the market. In 1986, Weston et al.¹⁹ provided the first US-based evidence that patch testing with a commercially available patch test device was safe in well, unaffected infants, children, and adolescents. In 2011, Jacob et al.²⁰ showed that the T.R.U.E. Test (SmartPractice, Phoenix, AZ), which is currently FDA approved for adults, is both safe and effective when used in afflicted pediatric

patients age 6 to 18 years. Further, in 2014, Jacob et al.⁷ developed a 20-allergen patch test series specifically targeted for the pediatric population with suspected ACD. Although the test is not all-inclusive, it serves as a basic screen that targets the most common allergens found in the 6- to 12-year-old sensitized population.⁷ Adjustments may be made to the concentration of certain allergens in pediatric testing to avoid an irritant reaction that could be interpreted as a false-positive rate for ACD (especially relevant



Figure 3. Positive patch test result showing a 3+ (strong positive) reaction.

in the pediatric population and in any patient with atopic dermatitis).²¹

It is important to be aware of the limitations of patch testing: in general, the sensitivity and specificity of patch testing are 70% and 80%, respectively.²² Therefore, clinical correlation with the test results is critical. Thimerosal remains a good illustration of this point, as it demonstrates a significant rate of positive patch test reactions that frequently lack clinical relevance.³ The high rates of irrelevant sensitization to this mercury derivative are thought to be partially due to its use as a vaccine preservative.

Another limitation to patch testing has been access to providers who are comfortable administering the test and interpreting the results. Fortunately, there are significant efforts underway to make the task of locating these providers easier. The ACDS houses a “find a provider” resource on their website.²³ Similar efforts are underway to create a resource for pe-

diatric patch test providers through the Loma Linda University Pediatric Contact Dermatitis registry.²⁴

COMPLICATIONS OF CONTACT DERMATITIS

Auto-Eczematization

In 2002, Silverberg et al.²⁵ analyzed 30 patch-tested pediatric patients, ages 1 to 18 years, who clinically were suspected to have nickel ACD. In over half the cases in this study, the patients suffered from an extensive systematized idiopathic reaction, with widespread dermatitis noted from localized direct and prolonged contact with a nickel-releasing agent (eg, earrings, belt buckle, etc).²⁵ Also known as auto-eczematization, this is a systemic flare of dermatitis after a previous bout of localized dermatitis. The pathophysiology is thought to be an autoimmune reaction to autologous skin antigens, with increased levels of circulating T cells.²⁶ In terms of quality of life, the idiopathic reaction can cause significant morbidity and persist for months.²⁵

Infection

Secondarily infected dermatitis is not unique to contact dermatitis, but it is a relevant and prevalent risk. Dermatitis both results from and causes disruption of the normal skin barrier. This disruption presents an opportunity for bacteria and other infectious agents to enter. Practitioners must be aware of this increased risk and advise patients to seek treatment for secondary infection if warranted.²⁷ In addition, patients with repeated significant secondary infections may require bleach baths and antibiotics to help prevent flares during patch testing and to support the protective effects of normal flora, such as *Staphylococcus epidermidis*.²⁷

Provocation of Atopic Dermatitis

Consider ACD in all children with refractory dermatitis, and especially in

those who have the diagnosis of atopic dermatitis. The innate barrier function defects in AD may predispose to sensitization through facilitated allergen penetration.²⁸ Of important note, the loss-of-function mutation in the *FLG* gene that predisposes people to clinically developing AD may also predispose them to the development of ACD.²⁹ Antimicrobial peptides (AMPs) may also play a role, as noted by the interventional effect of the addition of exogenous cathelicidin, which inhibits ACD *in vivo*.³⁰

Historically, a commonly held belief was that patients with AD, especially severe AD, had a depressed Th1 immune system and would therefore be protected from, or less likely to develop, ACD.³¹ A growing body of evidence is emerging that demonstrates that people with moderate to severe AD with chronic disease in fact express Th1 cytokines, and in these people there is a significant prevalence of ACD.³² Furthermore, this observed Th2 cytokine inhibition in people with moderate to severe AD is associated with decreased expression of cathelicidins and subsequent loss of their anti-inflammatory effects and lack of the antimicrobial effects of AMPs. Therefore, severe AD confers a greater likelihood of developing ACD by multiple mechanisms.

TREATMENT AND PREVENTION

For contact dermatitis, the backbone of treatment and prevention lies in avoidance of the exogenous offending substance. As a comprehensive review of adjunct therapeutic options is beyond the scope of this article, readers are directed to articles by Jacob and Castanedo-Tardan³³ and Cohen and Heidary.³⁴ With irritant contact dermatitis, the diagnosis is made through history and physical examination, and the treatment involves efforts to repair and restore skin barrier function while preventing further contact with the suspected offending substance. In cases

where avoidance is difficult (eg, urine or saliva-related dermatitis), the standard approach is to also include the use of exogenous barrier protectants, from silicone-derivative emollients to protective gear.

In ACD, the treatment is avoidance of the offending substance once the agent has been confirmed by patch testing. Allergen-specific education resources for patients are available online.³⁵ Furthermore, prevention of pediatric exposures to top allergens would represent a major public health intervention. Enforcement of prevention extends from the level of patient and provider education to national legislative initiatives. Removing nickel-releasing alloys from piercing posts available in the US market has the potential to save \$5.7 billion per year, but action at the federal level has yet to be taken.⁵

Efforts are underway to formulate a plan for nickel ACD prevention. In February of 2015, the ACDS and the Nickel Allergy Alliance endorsed a resolution recommending that the AAD Patient Safety and Quality Committee issue a health advisory regarding the high sensitization rates to nickel in the US.³⁶ They further called for mandatory regulations on the allowable quantity of nickel release from consumer-oriented products (similar to the directive enacted by the European Union [EU] in 1994). In August of 2015, the AAD issued a Position Statement on Nickel Sensitivity wherein the AAD highlights its commitment to reducing nickel allergy by limiting exposure and promoting public education.³⁷ In a 2015 publication, Jacob et al.⁵ called for legislation and effective enforcement to be undertaken to reduce the effects of nickel ACD in US children.

CONCLUSION

Contact dermatitis is a burdensome pediatric disease that leads to significant health and economic adversities.

Management of this disease requires the determination and elimination of the offending allergen. The cornerstone of prevention is to avoid potential sensitizers. Worldwide, nickel is the number one patch-tested allergen causing ACD. Since the European Union established safe use regulations for nickel in the mid-1990s, there have been dramatic reductions in related disease and costs in Europe. This European directive represents a compelling model and a pediatric prescription for more worldwide relief from ACD.

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