Actas Dermosifiliogr. 2011;**102(1)**:8–18

ACTAS
Dermo-Sifiliográficas

Full English text available at
www.elsevier.es/ad

REVIEW

Contact Dermatitis in Children – A Review of Current Opinions

M.P. Castanedo-Tardan,[a] C. Matiz,[b] S.E. Jacob[b,*]

[a]*Section of Dermatology, Dartmouth-Hitchcock Medical Center, Lebanon, NH, United States*
[b]*Division of Pediatric Dermatology, Rady Children's Hospital – UCSD, San Diego, CA, United States*

Manuscript received July 31, 2009; accepted for publication December 21, 2009

KEYWORDS
Allergic contact dermatitis;
Children;
Patch test

Abstract In the not so distant past, in the United States contact dermatitis was considered to be a condition that affected mainly adults. The diagnosis was certainly less often rendered in pediatrics, mainly because it was believed that a child's immune system was immature and that children were generally exposed to fewer allergens. With this in mind, we can attribute the low prevalence formerly reported for this disease partly to the fact that most affected children were not (and are still not) evaluated using appropriate skin tests. Patch testing in children requires certain modifications, but the international literature of the last decade and US data published in the past year indicate that contact dermatitis is a common condition in the pediatric population and that the prevalence is similar in children and adults.

PALABRAS CLAVE
Dermatitis de contacto alérgica;
Niños;
Prueba del parche

Dermatitis por contacto en Pediatría: revisión de opiniones actuales

Resumen En un pasado no muy distante, en los Estados Unidos de América se consideraba la dermatitis por contacto una entidad que afectaba principalmente a la población adulta. Este diagnóstico era distintivamente menos habitual entre niños, comparado con adultos, principalmente debido a la creencia de que en los niños, el sistema inmune era inmaduro y que en general estaban expuestos a una menor cantidad de alérgenos. Con esto en mente, la baja prevalencia comunicada en el pasado se debe también en parte a que la mayoría de los niños afectados no fueron, y aún no son, apropiadamente evaluados por medio de pruebas epicutáneas. Mientras que la prueba del parche en niños requiere ciertas modificaciones de la técnica, la información internacional de la última década, y los datos estadounidenses comunicados en el último año, indican que la dermatitis por contacto en la población pediátrica es una condición común e igualmente prevalente en niños que en adultos.

*Corresponding author.
E-mail address: sjacob@contactderm.net (S.E. Jacob).

Introduction

Not so long ago, in the United States, contact dermatitis was considered as a condition that affected mainly adults. It was diagnosed much less often in children compared to adults, essentially because dermatologists believed that the immune system in children was immature and that children were generally exposed to fewer allergens. The low prevalence reported in the past may therefore be attributed in part to the fact that most affected children did not (and still do not) undergo appropriate evaluation by patch testing. While patch testing requires certain adaptations for use in children, international experience from the past decade and US data reported in the past year indicate that contact dermatitis in children is widespread and in fact just as prevalent as in adults.[1]

Prevalence of Contact Dermatitis in Children

Allergic contact dermatitis and irritant contact dermatitis have been shown to occur in children. Recent data show that allergic contact dermatitis accounts for up to 20% of all forms of dermatitis in children.[2,3] Despite extensive information available in the literature, the real incidence and prevalence of contact allergy (sensitization) and allergic contact dermatitis in children and adolescents is largely unknown. The point prevalence of contact allergy (positive patch test in an asymptomatic patient) varies between 13% and 24%,[4-6] which is considerably lower than the prevalence in selected pediatric populations (symptomatic patients). Thus, the real prevalence of allergic contact dermatitis (defined as a positive patch test with clinical correlation with the dermatitis experienced by a symptomatic individual) ranges from 14% to 77% among children referred for patch testing due to clinical suspicion of contact dermatitis.[1,7-9]

Most studies of allergic contact dermatitis in children have been performed by European centers,[1,5,6,8] with only a few performed in North America.[10,11] It is difficult to compare the results because studies generally use distinct criteria in their design, specifying different age groups, concentrations of chemicals studied, and duration of the patch application.[12] Nevertheless, based on the available studies, allergic contact dermatitis is widely suspected to be increasing in the pediatric population.[13]

Diagnosis

The first step in the diagnosis of allergic contact dermatitis is to record a detailed medical and environmental history for the child (Table 1). To arrive at a diagnosis, strong suspicion is required given that allergic contact dermatitis may be difficult to differentiate clinically and pathologically from other eczematous dermatoses. In addition, allergic contact dermatitis does not always present clinically as eczema.

Allergic contact dermatitis in children always forms part of the differential diagnosis of any type of chronic or persistent dermatitis or one that worsens despite appropriate treatment. However, in the United States, given that most children with chronic dermatitis are not assessed using patch testing, there are no reliable figures on the exact prevalence of allergic contact dermatitis in the pediatric population.[14] This is certainly unfortunate because patch testing can help to identify the responsible allergen and it has been shown that identification of the culprit and subsequent contact allergen avoidance can improve the symptoms of allergic contact dermatitis, along with the quality of life of the patients.[15]

Patch Testing in Children

The patch test, also known as the epicutaneous test, is considered the gold standard for diagnosis of allergic contact dermatitis, and should be performed when there is clinical suspicion or a patient history suggestive of the condition. In the United States, 2 kits are available commercially and approved by the US Food and Drug Administration (FDA) as diagnostic tools in the adult population: the Thin-layer Rapid Use Epicutaneous Test (TRUE test), which contains up to 28 allergens plus a negative control and is available as 3 different panels (panels 1.1, 2.1, and 3.1), and the Hermal/Trolab test, which comprises 20 allergens. At the time of writing, neither of these diagnostic tests had been approved for use in children in the United States. In addition, they contain a limited number of allergens; thus, many cases of allergic contact dermatitis in children may go undetected.[16]

A comprehensive patch test can, however, be elaborated according to the specific needs of each patient; the number of allergens and their nature are selected according to the medical history and specific distribution of dermatitis in each patient.

Not only are these standard kits not approved for use in children, but Jacob et al[17] also found that a significant number of positive reactions observed in patients examined by comprehensive patch testing with expanded batteries of allergens would not have been detected using only the standard panels of the TRUE test or the Hermal test. Thus, Zug et al[10] highlight the importance of using expanded allergen panels in children who do not improve after initial study with the TRUE test.

The most common adverse effects of patch testing include adverse reactions at the site of positive reaction to the tested allergen, pruritus, burning, edema, erythema, vesicular reactions, and, less frequently, hypopigmentation or hyperpigmentation, or excessive duration of a positive reaction. Reactivation of dermatitis at previously affected sites is common and not considered an adverse reaction. If we apply the results of studies in adult populations to children, the possibility of generating active sensitization by application of allergens in patch testing is very low.[16] Other more serious adverse effects, such as anaphylactoid reactions, are rare.

Protocol for Patch Testing: Allergen Selection and Interpretation of the Results

There is no standard universally accepted allergen panel for either adult or pediatric use; however, the standard panels can be used as a starting point for allergen selection.

Table 1 Evaluation Necessary for Diagnosis of Allergic Contact Dermatitis in Children

I. High Clinical Suspicion in the Following Circumstances:
- New dermatitis with a nonatopic distribution (localized and/or persistent reactions on the hands, feet, and around the mouth)
- Worsening of constitutional dermatoses
- Dyshidrosis of hands and feet
- Dermatitis unresponsive to standard therapies

II. Detailed Medical History Based on:
- Patient demographics (age, sex, history of atopy, etc)
- Medical history and prior medication
- Personal hygiene products used by the child (shampoo, soap, wipes, etc)
- Household environment (personal hygiene products used by the parents, etc)
- Environments where the child spends time (school, playground, home—chairs and desks used at school, mattresses, hygiene products—etc)
- Sports or hobbies (baseball, hockey, American football, diving, painting, sculpting, etc)
- Temporal relationship of dermatitis with environmental exposure (by means of medical history)

III. Physical Examination and Overall Examination:
- Body distribution of dermatitis
- Important negative findings

IV. Selection of Allergens That Have to Be Evaluated Taking Into Account:
- The limited area for applying the patches given the small surface area of children's backs
- Selection of most likely allergens based on the history of recurrent exposure to the same allergen from one or more sources[a]

V. Selection and Application of Allergens:
- Use of the smallest amounts of allergen possible without compromising the ability to detect the clinically relevant allergen[b]
- Application of patches to the back (and the inner arm if necessary)
- Change the patches after 24-48 h
- Evaluation after 48 and 72 h

VI. Establish Clinical Relevance:
- Identify the most likely culprit allergens for the clinical findings
- Identify which of the allergens is present in the environment of the affected child

VII. Devise a Strategy to Avoid Contact With Responsible Allergens

[a]This is part of the "art": for example, markers of allergy to fragrances or flavoring such as a) fragrance mix I or II; or b) *Myroxylon pereirae* (balsam of Peru) should be included in patch testing if the mother uses fragrances, if fragrances are present in personal hygiene products used by the child (for example shampoo, body lotion, bubble bath), or if the child often ingests flavoring agents (for example, tomato ketchup, cinnamon, vanilla, etc).

[b]This is the "trick": being able to examine the patient with an extensive panel—integral and personalized—that helps identify allergens responsible for the dermatitis despite the small surface area of children's backs. Evaluation by means of patches in children—Recommendations of the German Contact Dermatitis Research Group (DKG).[22] Adapted from Jacob SE et al.[28]

Careful, individualized selection of the allergens suspected to be responsible for dermatitis should be based on the symptoms and history of exposure of each individual with suspected allergic contact dermatitis.

The different clinical groups regularly update their standard panels and adapt them according to the most commonly detected allergens in their base population.[18] Regardless of the panels chosen, it is important to bear in mind that new products with potentially allergenic ingredients are constantly being introduced to the market, and that sources of exposure to the same chemical generally vary among individuals, making it necessary to continually review and update the standard panels.[18]

Examples of the different pediatric panels suggested for detection in children with suspicion of allergic contact dermatitis include the following: standard abbreviated panels for children designed by Roul et al[19]; the so-called pediatric series developed by Manzini et al,[20] which comprised the 31 most common sensitizing substances in children evaluated in their Italian clinic; the standard series for evaluation of allergic contact dermatitis in children proposed by Hogan and Weston[21]; the base

pediatric screening panel developed by Jacob,[17] to which allergens can be added for performing patch testing in children in the United States; the panel proposed by the North American Contact Dermatitis Group (NACDG),[10] which consists of the 45 allergens that were most frequently positive and relevant in studies in children; and the standard 12-allergen panel for children between 6 and 12 years old, recommended by the German Contact Dermatitis Research Group (DKG)[22] (Table 2).

All these panels provide a guide for study of allergic contact dermatitis in children and point to those allergens which are most likely to give a positive result according to the place of residence and specific population attended by each clinic. In addition, they support the fact that the choice of allergens should be based on the clinical presentation and the individual history of each patient. Many authors also suggest the inclusion of supplementary allergens which form part of extended specialty panels (such as, for example, vehicles, textile dyes, plastics, and glues) based on clinical suspicion, and point to the importance of testing children with their own personal hygiene products (such as diaper creams or talc) as well as any topical medication in use (creams, lotions, or ointments) when considered potentially relevant.

Special Considerations for Patch Testing in Children

Patch application site. One of the intrinsic problems with patch testing in children is that their backs have a small surface area (Figure 1). In some cases, allergens (individually selected) may be applied not only to the back but also to the flexural areas of the arms. Alternatively, they can be applied in 2 different sessions 1 month apart.[23] As children are very active, special care should be taken to protect the patches with gauze strips or special clothing. The use of games or videos to distract the children during patch application can also be very helpful.[24]

Allergen concentration. The concentrations at which the allergens are studied in children is a subject of debate. Whereas most studies suggest that the same concentration used in adults should be applied in children,[23] atypical irritant reactions have been reported, particularly in the youngest patients.[25] Thus, Marcussen[26] found that nickel sulfate and formaldehyde at nonirritant dilutions in adults "gave a high percentage of primary irritant reactions in children." In that study, the percentage of irritant reactions decreased with increasing age, and disappeared between 7 and 10 years of age.

In a similar attempt to reduce the rate of false-positive readings due to irritant reactions, Fisher[27] recommended halving the concentrations of certain chemicals, and of formaldehyde and nickel in particular, in children under 8 years old (from the usual 5% nickel sulfate concentration in petroleum jelly used in adults to 2.5%, and from the aqueous 1% formaldehyde concentration to 0.5%). In the same article, the author also proposed that formaldehyde-releasing preservatives should be tested at half the concentration usually used in patch testing in adults, and that rubber additives (antioxidants and accelerators) such as mercaptobenzothiazole and thiuram mixes should also be tested at half the concentration in children under

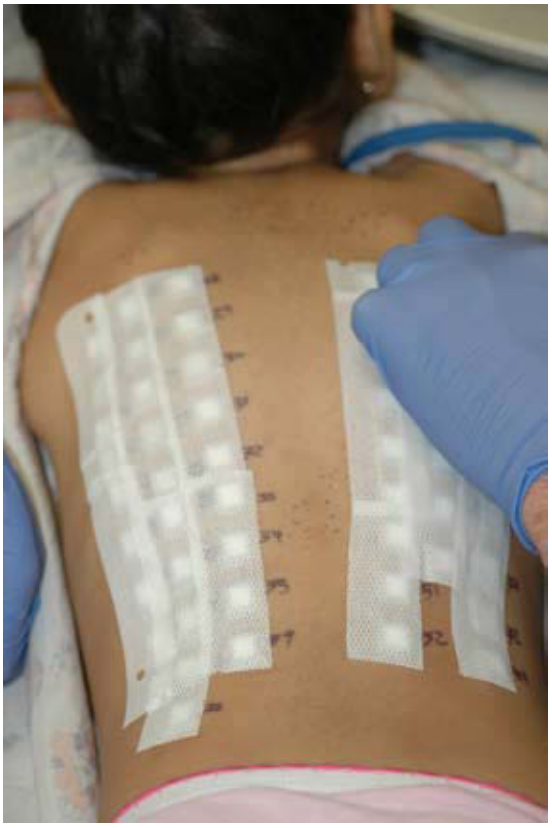

Figure 1. Application of patch test to a 3-year-old girl.

10 years of age. Fisher reiterated that patch testing in children requires careful interpretation as the standard concentrations of chemicals used in adults may lead to nonspecific irritant reactions in children.[27]

The protocol for the patch test of Jacob et al[28] modified the recommendations of Fisher and applied them to children under 5 years old. It was also proposed to dilute *p*-phenylenediamine (PPD) to half the concentration used in adults. The rationale behind these changes was that those authors were able to induce positive and relevant reactions in children using the lower concentrations.

Rietschel and Rosenthal[29] retrospectively examined the findings of the NACDG between 1984 and 1987 in search of irritant reactions caused by patch testing. In their analysis, 11% of the irritant reactions occurred in individuals aged over 80 years and 9% in those aged between 20 and 64 years, but none were found in the 0-12–year age group. The authors thus concluded that it is not necessary to modify the concentrations used in adults when patch testing children. This conclusion is supported by other studies.[29,30] In 1999, Mortz and Andersen[31] reviewed 17 studies of allergic contact dermatitis in children (5728 children in total) and concluded that the "general opinion today is that children can be patch tested with the same concentrations as adults."

Reading time points. Another aspect of patch testing in children about which there is a lack of consensus in

Table 2 Pediatric Patch Test Panels Proposed for Diagnosis of Children With Suspected Allergic Contact Dermatitis

	Hogan and Weston[21]	Manzini et al[20]	Fernández Vozmediano et al[1]	Roul et al[19]	DKG[22]	Jacob et al[17]	NACDG[10]
Year	1993	1998	2000	1999	2007	2008	2008
Population	United States	Italy	Spain	France	Germany	United States	European Union and Canada
Number of allergens proposed	20	- First series: 31 - Second series: 15	27 (standard GEIDAC battery)	- Children ≤ 6 years: 17 - Children > 6 years: 29 (shortened standard European series)	- Children 6-12: 12 - 5 additional allergens if positive history or suggestive clinical presentation[a]	40	45
Allergen concentration	Half concentration for nickel, potassium dichromate, MBT, and mercapto mix	Same concentration as in adults	Same concentration as in adults	Same concentration as in adults	Same concentration as in adults	Half concentration for nickel, formaldehyde, MBT, PPD, and mercapto, carba and thiuram mixes in children ≤ 5	Same concentration as in adults
List of allergens and suggested concentrations (dilution in petroleum jelly unless otherwise specified)	Benzocaine 5% midazolidinyl urea 2% Thiuram mix 1% Lanolin 30% Neomycin sulfate 20% PPD 1% MBT 1% PTBP-F-R 1% Cinnamic aldehyde 1% Formaldehyde 1% aq Carba mix 3% Colophony 20% PPD mix 0.6% EDDI 1% Quaternium-15 2% Mercapto mix 1%	*First series* Potassium dichromate Nickel PPD Formaldehyde EDDI MBT Thiuram mix PTBP-F-R Balsam of Peru Neomycin Benzocaine Lanolin Paraben mix Colophony Propolis	Nickel sulfate 5% Wool alcohols 30% Neomycin sulfate 20% Potassium dichromate 0.5% Benzocaine 5% Fragrance mix 8% Colophony 20% Epoxy resin 1% Balsam of Peru 25% Cobalt chloride 1% PTBP-F-R 1% Paraben mix 16% aq Carbamate mix 3% PPD 0.1% Kathon CG (CMI/MI) 100 ppm	Potassium dichromate 0.5% Neomycin sulfate 20% Thiuram mix 1% Formaldehyde 1% aq Colophony 20% Balsam of Peru 25% Lanolin 30% Paraben mix 15% PTBP-F-R 1% Fragrance mix 8% Nickel sulfate 5% MBT 2% Thimerosal 0.1% Petroleum jelly (control)	Nickel sulfate 5% Thiuram mix 1% Colophony 20% MBT 2% Fragrance mix I 8% Fragrance mix II 14% Mercapto mix 1% Bufexamac 5% Euxyl K400 1% CMI/MI ppm aq Neomycin 20% Compositae mix 6% PTBP-F-R 1% Potassium dichromate 0.5% Lanolin 30%	Bacitracin 20% Balsam of Peru (*Myroxylon pereirae*) 25% Benzocaine 5% Benzophenone-3 3% Benzoyl alcohol 1% Bronopol 0.5% Budesonide 1% Carba mix 3% Cinnamic aldehyde 1% Cobalt chloride 1% Cocamidopropyl betaine 1% aq Colophony 20% Compositae mix 6%	Nickel sulfate 2.5% Cobalt chloride 1% Thimerosal 0.1% Neomycin sulfate 20% Gold and sodium thiosulfate 0.5% Fragrance mix I 8% *Myroxylon pereirae* 25% Quaternium-15 2% Lanolin alcohol 30% Potassium dichromate 0.25% Colophony 20%

Table 2 *(Continued)*

	Hogan and Weston[21]	Manzini et al[20]	Fernández Vozmediano et al[1]	Roul et al[19]	DKG[22]	Jacob et al[17]	NACDG[10]
	Epoxy resin 1% Balsam of Peru 25% Potassium dichromate 0.25% Nickel sulfate 2.5%	Fragrance mix MBT mix 2% Diaminodiphenylmethane (DDM) Ammoniated mercury Turpentine Imidazolidinyl urea CMI/MI (Kathon CG) Hydroquinone Thimerosal Disperse yellow 3 Disperse red 1 Disperse orange 3 Disperse blue 124 *p*-dimethylamino-azobenzene Euxyl K 400 2.5% Span 20 *Second series* Epoxy resin N-isopropyl-N'-phenyl-*p*-phenylenediamine Diazolidinyl urea Quaternium-15 Oleamidopropyl dimethylamine Dimethylamino-propylamine Disperse blue 106 *p*-aminoazobenzene Butyl methoxyphenol Fragrance mix + sorbitan sesquioleate Span 80 5%	Quaternium-15 1% MBT 2% Thimerosal 0.1% EDDI 1% Formaldehyde 1% Thiuram mix 1% Tixocortol pivalate 0.1% Thiuram mix 1% Budesonide 1% Eukyl K400 0.5% Lactone mix 0.1%	Tixocortol pivalate Budesonide Fusidic acid 2% EDDI 1% PPD 1% Cobalt chloride 1% N-isopropyl-N'-phenyl-*p*-phenylene-diamine 0.1% Mercapto mix 2% Epoxy resin 1% Quaternium-15 1% Kathon CG (CMI/MI) Hydrocortisone-17-butyrate Lactone mix Betamethasone-17-valerate Clobetasol-17-propionate	Disperse blue mix 1% PPD 0.5%	Diazolidinyl urea 2% Disperse blue mix 124/106 1% Disperse yellow mix 3/9 DMDM hydantoin 1% Epoxy resin 1% EDDI 1% Euxyl K400 2% Formaldehyde 1% aq Fragrance mix I 8% Fragrance mix II 14% Imidazolidinyl urea 2% Lanolin 30% MBT 1% Mercapto mix 1% CMI/MI 100 ppm aq Neomycin sulfate 20% Nickel sulfate 5% PTBP-F-R 1% Paraben mix 12% PPD 1% Potassium dichromate 0.25% Propolis (bee resin) 10% Propylene glycol 30% aq	Bacitracin 20% Propylene glycol 30% aq Formaldehyde 1% aq Benzalkonium chloride 0.1% aq PPD 1% Disperse blue 106 1% Diazolidinyl urea 1% aq MBT 1% Carbamate mix 3% Thiuram mix 1% Budesonide 0.01% Compositae mix 6% Amidoamine 0.1% Cocamidopropyl betaine 1% aq Bronopol 0.5% EDDI 1.0% Di-α tocopherol 100% Imidazolidinyl urea 1% CMI/MI ppm aq Ethylene urea melamine formaldehyde 5% PTBP-F-R 1% Oxidized tea tree oil 5% Clobetasol-17-propionate 1% Thiourea mix 1% Budesonide 0.1% Pure jasmine oil 2% Mercapto mix 1%

Table 2 *(Continued)*

	Hogan and Weston[21]	Manzini et al[20]	Fernández Vozmediano et al[1]	Roul et al[19]	DKG[22]	Jacob et al[17]	NACDG[10]
		Hydrocortisone-17-butyrate Betamethasone-17-valerate Budesonide Tixocortol pivalate				Quaternium-15 2% Thiurams 1% Tixocortol pivalate 0.1% TFR 10%	Tetracaine 1% Ylang-ylang oil 2% IPBC 0.1% DMDM hydantoin 1% aq TFR 10% Euxyl K400 2%

Modified from Jacob SE et al.[28] [a]Evaluation by patch testing in children—Recommendations of the German Contact Dermatitis Research Group (DKG).[22] Myroxylon pereirae is Balsam of Peru. Quaternium-15, diazolidinyl urea, imidazolidinyl urea, bronopol and DMDM hydantoin comprise a group of preservatives known as formaldehyde-releasing preservatives.
Abbreviations: bronopol, 2-bromo-2-nitropropane-1,3-diol; CMI/MI, 5-chloro-2-methyl-3-isothiazolone / 2-methyl-3-isothiazolone (Kathon CG); DMDM hydantoin, dimethylol-5,5-dimethylhydantoin; EDDI, ethylenediamine dihydriodide; Euxyl K 400 (dibromodicyanobutane), methyldibromo glutaronitrile/phenoxyethanol; GEIDAC, Spanish Contact Dermatitis Research Group; IPBC, iodopropynyl butylcarbamate; lanolin, wool alcohols and lanolin alcohols; MBT, mercaptobenzothiazole; NACDG, North American Contact Dermatitis Group; p-dimethylaminoazobenzene, butter yellow; PPD, p-phenylenediamine; PTBP-F-R, p-tert-butylphenol-formaldehyde resin; span 20, sorbitan monolaurate; span 80, sorbitan monooleate; TFR, tosylamide/formaldehyde resin (toluene).

the literature is the appropriate moment for evaluating the test (reaction reading). Most authors agree that the patches should be applied to healthy skin on the back, and should be kept occluded for 48 hours. In most studies in children, 2 readings are taken: on the day the patches are removed, that is, 48 hours after application (day 2) and then 96 hours after application (day 4). However, 1 study recommended that the patches remain occluded for 72 hours and that a single reading be performed after 72 hours[22] (the potential for active sensitization of more prolonged exposure has not been investigated in children). Jacob et al[17] evaluated all patients under 5 yeas of age at 48, 72, and 96 hours after patch application, and found no difference between readings at 72 and 96 hours. In contrast, the DKG[22] proposed that patches be removed after 24 hours in children under 12 years of age to reduce the frequency of irritant reactions and that readings be taken at 48 and 72 hours. In line with the German protocol, Jacob et al[28] suggested that a delayed reading at 72 hours (and not at 96 hours) would suffice.

Morphology of the reaction. Regardless of the timing of the reading, the result is reported as positive or negative, with positive results classified using a quantitative scale. The International Contact Dermatitis Research Group (ICDRG) recommended a grading system from + to +++, where + indicates redness without swelling, ++ indicates redness, swollen skin, and blisters, and +++ represents a severe reaction (blistering). The faintest or least clear reactions are recorded with a question mark (?), while irritant reactions are recorded as "IR". According to Rietschel and Fowler,[32] irritant reactions are the bane of the patch test given that they are difficult to interpret. Although many text books indicate that the evaluator may correctly decide whether a patch test reaction is irritant or allergic according to its shape alone, in actual fact, the morphology of a patch test reaction is usually a poor guide as to whether the response is allergic or irritant. In general, an intense irritant reaction to the patch test will appear early on (at the first reading), have well-defined edges (similar to a burn), and disappear quickly (the reaction is very weak or not present at all at the second reading). In contrast, an intense allergic reaction is usually more diffuse, disappears more slowly, and is clearly eczematous. Nevertheless, there is no well-defined approach based on evaluation of morphology that can accurately distinguish between a weak irritant test and a week allergic test.[32]

Relevance. One of the most important aspects of patch testing in children is how to interpret the results. It is critical to establish the clinical relevance of a positive result because, according to Mortz and Andersen,[31] there is only a "partial concordance" between a positive patch test and allergic contact dermatitis. A positive patch test does not confirm the presence of allergic contact dermatitis. For this reason there are 2 different terms to define a positive patch test according to the clinical relevance. Allergic contact dermatitis refers to the clinical disease in the context of a positive patch test that is also clinically relevant. The allergen that tests positive therefore contributes to the dermatitis of a symptomatic patient. On the other hand, contact allergy is a positive patch test that is not clinically relevant for the dermatitis of the symptomatic patient, or a positive patch test observed in an asymptomatic individual (for example, in those studies in the healthy population in which the prevalence of sensitization and not disease is examined).

Clinical relevance is therefore essential for a diagnosis of allergic contact dermatitis. In general, assigning clinical relevance depends on experience and the amount of effort the dermatologist and the parents of the patient are prepared to make. The relevance of a positive reaction is generally recorded as current (and can be classified as definitive, probable, or possible), past, uncertain, or not pertinent. Relevance is considered definitive if a provocative use test (see below) or a patch test with a product/object that contains the suspected allergen (for example, diaper cream or a piece of shoe) is positive.[33] Relevance is considered probable if the allergen identified by the patch test is present in the agents to which the skin of the patient has been exposed. Finally, the relevance is considered possible if the patient may have been exposed to circumstances in which the skin has come into contact with certain materials that are known to contain the responsible agent.

Certain techniques may help establish the clinical relevance. One is to assess the patient some time after application of the patch test to verify whether there has been improvement after allergen avoidance. Another is to instruct the parents to perform a provocative use test at home. This consists of the patient using the product presumed to be responsible for the dermatitis in exactly the same way as when the dermatitis appeared[33] (for example, applying the diaper cream suspected as being responsible twice during the week to a small area, 1 cm × 1 cm, of the skin in contact with the diaper). If an eczematous reaction occurs during the test period, the test is considered positive and the clinical relevance is confirmed. Likewise, the so-called repeated open application test (ROAT) involves application of personal hygiene products that do not require rinsing, that is, products designed to stay in contact with the skin for a long time, such as lotions, creams, sunscreens, or lip salves. These are applied twice a day for a week to a 1 cm × 1 cm marked area of skin on the upper arm. This area is then examined daily for eczematous reactions.[34]

A key part of the protocol in pediatric departments is an educational session before patch application. The aim is to educate the parents about the nature of contact dermatitis and the importance of allergen avoidance once the culprit has been identified, in addition to providing realistic expectations concerning the result of the patch test, including the possibility that it might give a negative result. The parents should also be instructed on how to keep the patches dry by avoiding baths and any activity that might make the child sweat excessively. It is also important that the patients stop using medicines that might affect the test at least 2 weeks before it is carried out. This includes the use of topical corticosteroids or calcineurin inhibitors applied to the body area where the patches will be applied. Likewise, it should be explained to the parents that they will have to return the clinic twice, once to remove the patches and once for the final evaluation.

Table 3 List of the 10 Most Common Allergens in Children (USA, Canada, Europe, Brazil)

Allergen	Description	Source	Anatomical Distribution
Nickel sulfate	Metal	Jewelry, buttons and broaches, glasses, dental material, mobile phones, keys, coins	Face/eyelids, ears, neck, wrists
Neomycin	Topical antibiotic	Antibiotic ointment	Face, eyelids
Myroxylon pereirae (balsam of Peru)/ fragrance mix	Fragrances	Perfumes and cosmetics, toothpaste, mouth rinses, flavorings, tomatoes	Eyelids/face, neck, mouth, and lips
Thimerosal	Preservative	Vaccines, cosmetics, antiseptics	Body and torso
Potassium dichromate	Metal	Dyed leather, matches, cement, dental implants, green baize	Hands and periumbilical area
Cobalt	Metal	Jewelry, buttons, broaches, ceramics, cement, vitamin B_{12}	Ears, neck, periumbilical area, hands
Thiuram mix	Rubber accelerator	Elastic waists of clothing, tights, swimming suits, shoes (soles and interior parts), gloves, pesticides	Waist, feet, hands
Lanolin	Emollient	Emollient, soaps, protective waxes, lip balms	Hands, any part of the body to which emollients are applied
Formaldehyde and formaldehyde-releasing products	Preservative	Shampoo, lotions, cosmetics, wrinkle-free clothing	Face, ears, hands, trunk
p-Phenylenediamine	Chemical oxidant	Dye for hair, adulterated black henna, tattoos	Hairline, ears, hands, tattoo sites

Source: References 10, 15, 17, 19, and 30-33.

Important Allergens in Childhood

Like adults, children are usually sensitized to allergens found everywhere, such as nickel and fragrances (Figures 2 and 3). Table 3 shows the 10 most common allergens detected by patch testing for which clinical relevance has been documented in international studies (from the United States, Canada, Europe [Germany, Italy, Great Britain, France, Spain, and Belgium], and Brazil).

Therapeutic Interventions

The most important therapeutic intervention is contact allergen avoidance.[35] Fortunately, the culprit can often be correctly identified by appropriate patch testing. Subsequent contact allergen avoidance can lead to sustained remission of the dermatitis. If patch testing fails to identify the responsible allergen and the diagnosis of allergic contact dermatitis is still suspected, a detailed diary of daily activities and products that the patient comes into contact with may help reveal certain types of exposure.

As mentioned earlier, a critical component for appropriate contact allergen avoidance, and therefore for the successful treatment of contact dermatitis in pediatric practice, is education of the patients and their families. Two of the most widespread methods for patient education are use of readily comprehensible information with details of the different allergens, where they are found, and how they can be avoided, followed by a face-to-face tutorial after the final test reading. This education allows the parents to properly implement the allergen avoidance regimen, provides them with techniques for the day-to-day management of the dermatitis of their children, and helps them deal with frustrating relapses.

To encourage adherence to medical advice, the patient should be provided with safe alternatives; it is therefore essential that the dermatologist be familiar with the

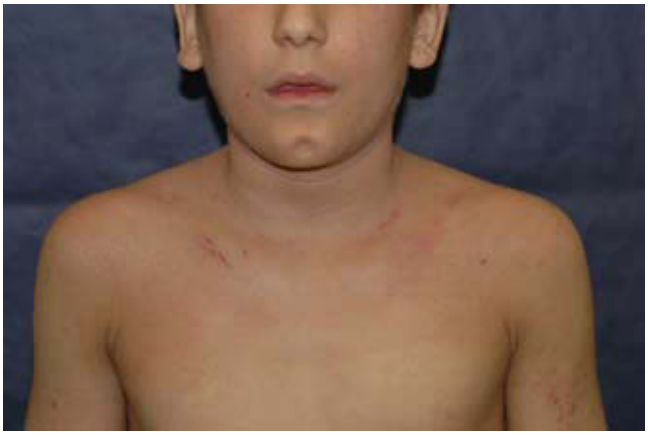

Figure 2 Ten-year-old boy with a year-long history of dermatitis confined to the face and neck caused by contact allergy to fragrances.

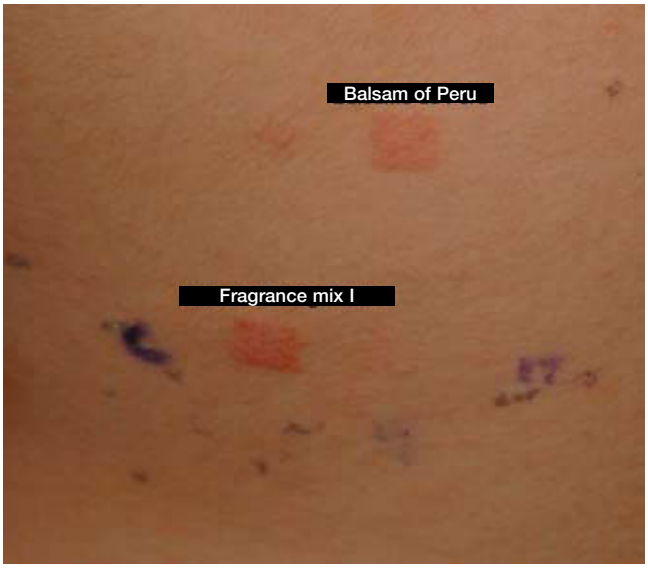

Figure 3 Positive patch test for fragrance mix I and balsam of Peru in the patient in Figure 2.

content of the different products that might be used to exclude chemicals to which the patient is allergic.

In those cases in which contact allergen avoidance has not led to improvement, topical and systemic treatments may be prescribed. Topical corticosteroids are effective, but may cause side effects in the long term[36-38] or may even be allergenic themselves. Topical calcineurin inhibitors can be used, particularly on areas such as the face and intertriginous areas. With particularly severe dermatitis, mucosal involvement, or persistence despite topical treatment, the use of systemic agents should be considered. In acute or severe cases, oral corticosteroids at doses of 1 mg/kg/d can be used.[39] It is important to remember that prednisone is a class A corticosteroid and that there have been reports of patients who develop systemic reactions after receiving oral prednisone.[40,41] These reactions may respond to high doses of this same corticosteroid or the dose may be reduced. Other nonsteroidal immunosuppressants include agents such as cyclosporin, methotrexate, and azathioprine; the reader is referred to other key resources for additional discussion in greater depth of the topic.[42-44]

Conflicts of Interest

Dr Jacob is an independent researcher for Smartchoice (Allerderm), the manufacturer of the TRUE test. The other authors declare that they have no conflicts of interest.

References

1. Fernández Vozmediano JM, Armario Hita JC. Allergic contact dermatitis in children. J Eur Acad Dermatol Venereol. 2005;19:42–6.
2. Fisher AA. Childhood allergic contact dermatitis. Cutis. 1975;15:635.
3. Weston WL, Weston JA. Allergic contact dermatitis in children. Am J Dis Child. 1984;138:932–6.
4. Weston WL, Weston JA, Kinoshita J, Kloepfer S, Carreon L, Toth S, et al. Prevalence of positive epicutaneous tests among infants, children, and adolescence. Pediatrics. 1986;78:1070–4.
5. Barros MA, Baptista A, Correia TM, Azevedo F. Patch testing in children: A study of 562 schoolchildren. Contact Dermatitis. 1991;25:156–9.
6. Mortz CG, Lauritsen JM, Binslev-Jensen C, Andersen KE. Contact allergy and allergic contact dermatitis in adolescents: prevalence measures and associations. The Odense adolescence cohort study on atopic diseases and dermatitis (TOACS). Acta Derm Venereol. 2002;82:352–8.
7. Bruckner AL, Weston WL, Morelli JG. Does sensitization to contact allergens begin in infancy? Pediatrics. 2000;105:e3.
8. Seidenari S, Giusti F, Pepe P, Mantovani L. Contact sensitization in 1094 children undergoing patch testing over a 7-year period. Pediatr Dermatol. 2005;22:1–5.
9. Lewis VJ, Statham BN, Chowdhury MMU. Allergic contact dermatitis in 191 consecutively patch tested children. Contact Dermatitis. 2004;51:155–6.
10. Zug KA, McGinley-Smith D, Warshaw EM, Taylor JS, Rietschel RL, Maibach HI, et al. Contact allergy in children referred for patch testing: North American Contact Dermatitis Group data, 2001-2004. Arch Dermatol. 2008;144:1329–36.
11. Hogelin M, Pratt M. Allergic contact dermatitis in children: the Ottawa hospital patch-testing clinic experience, 1996 to 2006. Dermatitis. 2008;19:86–9.
12. de Waard-van der Spek FB, Oranje AP. Patch tests in children with suspected allergic contact dermatitis: A prospective study and review of the literature. Dermatology. 2008.
13. Militello G, Jacob SE, Crawford GH. Allergic contact dermatitis in children. Curr Opin Pediatr. 2006;18:385–90.
14. Morren MA, Pryzbilla B, Bamelis M, et al. Atopic dermatitis: Triggering factors. J Am Acad Dermatol. 1994;1:467–73.
15. Rajagopalan R, Anderson R. Impact of patch testing on dermatology-specific quality of life in patients with allergic contact dermatitis. Am J Contact Dermat. 1997;8:215–21.

16. Jensen CD, Paulsen E, Andersen KE. Retrospective evaluation of the consequence of alleged patch test sensitization. Contact Dermatitis. 2006;55:30–5.
17. Jacob SE, Brod B, Crawford GH. Clinically relevant patch test reactions in children—a United States based study. Pediatr Dermatol. 2008;25:520–7.
18. Fisher AA. Contact Dermatitis. 2nd ed. Philadelphia: Lea and Febiger; 1973.
19. Roul S, Ducombs G, Taieb A. Usefulness of the European standard series for patch testing in children. A 3-year single-centre study of 337 patients. Contact Dermatitis. 1999;40: 232–5.
20. Manzini BM, Ferdani G, Simonetti V, Donini M, Seidenari S. Contact sensitization in children. Pediatr Dermatol. 1998;15:12–7.
21. Hogan PA, Weston WL. Allergic contact dermatitis in children. Pediatr Rev. 1993;14:240–3.
22. Worm M, Aberer W, Agathos M, Becker D, Brasch J, Fuchs T, et al., German Contact Dermatitis Research Group. Patch testing in children–recommendations of the German Contact Dermatitis Research Group (DKG). J Dtsch Dermatol Ges. 2007;5:107–9.
23. Lacahapelle JM, Maibach HI. Patch testing, prick testing – A practical guide. Berlin: Springer; 2003.
24. Jacob SE. Avoid the shriek with Shrek: video distraction assist for pediatric patch testing. Dermatitis. 2007;18:179–80.
25. Johnke H, Norberg LA, Vach W, Bindslev-Jensen C, Høst A, Andersen KE, et al. Reactivity to patch tests with nickel sulfate and fragrance mix in infants. Contact Dermatitis. 2004;51: 141–7.
26. Marcussen PV. Primary irritant patch test reactions in children. Arch Dermatol. 1982;87:378.
27. Fisher AA. Patch testing in children including early infancy. Cutis. 1994;54:387–8.
28. Jacob SE, Burk CJ, Connelly EA. Patch testing: another steroid-sparing agent to consider in children. Pediatr Dermatol. 2008;25:81–7.
29. Rietschel RL, Rosenthal LE, NACDG. Standard patch test screening series used diagnostically in young and elderly patients. Am J Contact Derm. 1990;1:53–5.
30. Camarasa JMG, Aspiolea F, Alomar A. Patch tests to metals in childhood. Contact Dermatitis. 1983;9:157–8.
31. Mortz C, Andersen KE. Allergic contact dermatitis in children and adolescents. Contact Dermatitis. 1999;41:121–30.
32. Rietschel RL, Fowler Jr JF. Fisher's Contact Dermatitis. 6th ed. Ontario: BC Decker Inc, Hamilton; 20.
33. Bashir SJ, Maibach HI. Contact Urticaria Syndrome. In: Chew AL, Maibach HI, editors. Irritant Dermatitis. Berlin, Germany: Springer; 2006. p. 63–70.
34. Gelpi CB, Jacob SE. Instructions for educating patients on ROAT testing in conjunction with patch testing. Dermatol Nurs. 2008;20:139–43.
35. Jacob SE, Castanedo-Tardan MP. Pharmacotherapy for allergic contact dermatitis. Expert Opin Pharmacother. 2007;8:2757–74.
36. Cohen DE, Heidary N. Treatment of irritant and allergic contact dermatitis. Dermatologic Ther. 2004;17:334–40.
37. Hengge UR, Ruzicka T, Schwartz RA, Cork MJ. Adverse effects of topical glucocorticosteroids. J Am Acad Dermatol. 2006;54:1–15.
38. Mills CM, Marks R. Side effects of topical glucocorticoids. Curr Probl Dermatol. 1993;21:122–31.
39. Sidbury R, Hanifin JM. Systemic therapy of atopic dermatitis. Clin Exp Dermatol. 2000;25:559–66.
40. Fernández de Corres L, Bernaola G, Urrutia I, Munoz D. Allergic dermatitis from systemic treatment with corticosteroids. Contact Dermatitis. 1990;22:104–6.
41. Bircher AJ, Bigliardi P, Zaugg T, Mäkinen, Kiljunen S. Delayed generalized allergic reactions to corticosteroids. Dermatology. 2000;200:349–51.
42. Downs AM, Sansom JE. Severe contact allergy to footwear responding to handmade shoes. Contact Dermatitis. 1999;40: 218.
43. Sharma VK, Bhat R, Sethuraman G, Manchanda Y. Treatment of parthenium dermatitis with methotrexate. Contact Dermatitis. 2007;57:118–9.
44. Ricci G, Dondi A, Patrizi A, Masi M. Systemic therapy of atopic dermatitis in children. Drugs. 2009;69:297–306.