

# European Standard Series Patch Test Results in Pediatric Allergic Contact Dermatitis Patients: A Single-Center Experience

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## ABSTRACT

**Background:** Allergic contact dermatitis (ACD) is a Type IV hypersensitivity reaction that can be challenging to diagnose in children due to its resemblance to other dermatologic conditions such as atopic dermatitis. Despite historical beliefs, recent studies show that ACD is prevalent in pediatric populations, with an increasing number of cases reported.

**Objective:** This study aimed to investigate the prevalence of allergic sensitization in children with suspected ACD, identify the most common allergens, and examine the relationship between allergic diseases and patch test positivity.

**Materials and Methods:** A retrospective study was conducted at the Pediatric Allergy and Immunology Clinic between April 2023 and December 2024, including children aged 2–18 years. Patients underwent patch testing using the European standard series and were assessed for demographic data, allergic disease history, and laboratory tests.

**Results:** A total of 99 patients with suspected allergic contact dermatitis (ACD) were evaluated, with a median age of 14 years (IQR: 9–16). Patch test positivity was detected in 58 patients (58.6%), and clinically relevant sensitizations were identified in 32 of them (55.1%). The most commonly affected site was the hand (44%), frequently associated with metal exposure. At least one allergic disease was present in 50.5% of the patients, with atopic dermatitis (34.4%) being the most prevalent. Skin prick test positivity was observed in 28% of the patients, predominantly to pollen (22.2%). The most frequently detected contact allergens were metals (26.8%), particularly nickel sulfate (11.8%).

**Conclusion:** ACD is a common condition in children, with metals and preservatives as the most prevalent allergens. Early diagnosis through patch testing and proactive management of environmental exposures are crucial for improving patient outcomes and reducing the impact of ACD on the quality of life.

**Keywords:** Patch test, European Standard Series, Allergic Contact Dermatitis, Pediatric

## INTRODUCTION

Allergic Contact Dermatitis (ACD) is a delayed-type hypersensitivity reaction (Type IV hypersensitivity) that occurs when the skin comes into contact with an allergen, leading to an exaggerated immune response. Unlike immediate allergic reactions (such as urticaria or anaphylaxis),

ACD develops gradually over 24 to 72 hours after exposure. This condition is characterized by redness, itching, swelling, and sometimes blistering, particularly at the site of contact with the allergen (1). ACD is a common dermatologic condition that can be particularly challenging to diagnose in children due to several factors. It often mimics

or coexists with atopic dermatitis (AD), a prevalent childhood skin condition, leading clinicians to delay or avoid diagnostic testing in younger patients (2). ACD may also be difficult to distinguish from AD due to the high prevalence of AD in children.

While children are exposed to many of the same allergens as adults, their environmental exposures and sensitivities can differ due to age-specific factors (3). Additionally, the limited availability of unaffected skin for testing makes diagnosis in children more challenging. Previously, ACD was thought to be rare in children due to their immature immune systems and limited allergen exposure. However, recent data indicate that its prevalence is comparable to that in adults. (4). Even infants as young as one week old have been reported to develop ACD, underscoring the importance of recognizing and diagnosing the condition in pediatric patients.

ACD is a biphasic, type IV hypersensitivity reaction of the skin. In the sensitization phase, initial exposure to an allergen leads to its processing in regional lymph nodes and the formation of antigen-specific T cells. In the elicitation phase, re-exposure to the allergen triggers an inflammatory response, resulting in erythema, vesiculation, pruritus, and edema (5). Given these challenges, history and physical examination play a crucial role in assessing children for potential ACD. Patch testing remains the gold standard for diagnosis in pediatric patients, despite the difficulties associated with limited unaffected skin available for testing (6).

Children are frequently exposed to various allergens that can lead to ACD. Common pediatric allergens including metals, preservatives, and fragrances are also frequent triggers. Identifying and managing these allergens through patch testing is essential for effective prevention and treatment (7).

In our study, we aimed to evaluate the ESS (European Standard Series) patch test results applied with the preliminary diagnosis of ACD in the childhood age group and their compatibility with clinical findings.

## **MATERIAL and METHODS**

### **Study Design and Population**

This retrospective study included children aged 2 to 18 years who were evaluated at the Pediatric Allergy and Im-

munology Clinic for suspicion of ACD between April 2023 and December 2024. The study protocol was approved by the Institutional Ethics Committee (TABED 1-25-1103).

### **Data Collection**

Medical history and demographic information, including age, sex, patient history, and family history of allergic diseases, were obtained from hospital records. The presence of AD, asthma, and allergic rhinitis was documented. AD was diagnosed based on the Hanifin and Rajka criteria (8).

### **Laboratory and Allergy Testing**

Laboratory examinations, including complete blood count and serum total IgE levels if available, as well as skin prick test results if performed, were recorded. The skin prick test included aeroallergens such as house dust mites, cockroaches, animal hair, mixed grasses, and tree pollens. The tests that had been performed were included in the analysis.

### **Patch Testing Procedure**

All patients were tested using the ESS test, which includes 30 allergens (Chemotechnique Diagnostics, Malmö, Sweden), and the IQ-Chamber test material (Chemotechnique IQ Chamber®; Chemotechnique Diagnostics). Patch testing was not performed on patients receiving systemic corticosteroids or other immunosuppressive treatments. These medications were discontinued at least one month before the procedure. Topical corticosteroids were discontinued at the test site at least seven days before the test. Patch tests were applied to the patients' backs, and caregivers provided written informed consent. During the three-day test period, patients were advised to avoid antihistamines and corticosteroid-containing creams (6).

### **Patch Test Evaluation**

The patches were removed after 48 hours, and the initial reading was conducted after a 15–20-minute waiting period. The results were evaluated using the standard scoring systems of the International and European Contact Dermatitis Research Groups (ICDRG and ECDRG)(9). The presence of erythema, indurations, and small vesicles was considered a positive test result. If no reaction was observed, it was deemed a negative result. Patients were re-evaluated at 72 hours.

### Statistical Analysis

SPSS 25 (IBM Corp, Armonk, NY) was used for statistical analyses. Descriptive data are presented as numbers and percentages for categorical data, mean  $\pm$  standard deviation (SD) for normally distributed continuous data, and as median and interquartile range (IQR) for non-normally distributed continuous data. The Chi-square test was used to compare nominal variables.

Univariate logistic regression analysis was performed to evaluate the association between independent variables and the outcome variable. Results of the logistic regres-

sion analysis are presented as odds ratios (OR) with 95% confidence intervals (CI). Statistical significance was set at  $p < 0.05$ .

### RESULTS

This study included a total of 99 patients suspected of having ACD, with a median age of 14 years (IQR: 9-16). The demographic and laboratory characteristics, such as eosinophil count, white blood cell count, and IgE levels, are summarized. Patch test results revealed that 58 patients (58.6%) tested positive for at least one allergen (see Table I for details).

**Table I. Demographic, Clinical, and Hematologic Characteristics of Contact Dermatitis Patients**

|  | Median (IQR)           |                |
|--|------------------------|----------------|
| Age (Year)   | 14 (9–16)              |                |
| Absolute Eosinophil Count (cells/ $\mu$ L)   | 150 (105–310)          |                |
| Eosinophil Count (%)   | 2.20 (1.30–4.20)       |                |
| White Blood Cell Count (cells/ $\mu$ L)  | 7320 (6357.5–9110)     |                |
| Total IgE Level (UI/mL)  | 75.30 (15.85–400.2)    |                |
| Clinical Characteristic  | Count (n)              | Percentage (%) |
| <b>Gender Distribution</b>   |                        |                |
| Female   | 61                     | 61             |
| <b>Lesion Location</b>   |                        |                |
| Hand   | 44                     | 44             |
| Face   | 18                     | 18             |
| Trunk  | 15                     | 15             |
| Foot/Leg   | 8                      | 8              |
| Arm  | 12                     | 12             |
| Scalp  | 2                      | 2.0            |
| <b>History of Atopic Dermatitis</b>  | 34                     | 34             |
| <b>Additional Allergic Disease (Asthma, Allergic Rhinitis, Atopic Dermatitis etc.)</b> | 50                     | 50             |
| <b>Skin Prick Test Aeroallergen Positivity</b>   |                        |                |
| Positive   | 28                     | 28             |
| <b>Specific IgE Aeroallergen Positivity</b>  |                        |                |
| Positive   | 24                     | 24             |
| Number of Positive Allergens   | Number of Patients (n) | Percentage (%) |
| Only 1 Allergen  | 19                     | 32.8           |
| 2 Allergens  | 20                     | 34.5           |
| 3 Allergens  | 8                      | 13.8           |
| 4 Allergens  | 9                      | 15.5           |
| 5 Allergens  | 2                      | 3.4            |
| Total  | 58                     | 100            |

Among them, the most commonly affected body site was the hand (44.0%), followed by the face (18.0%), trunk (15.0%), and arm (12.0%). Less frequently affected areas included the foot/leg (8.0%) and scalp (2.0%). The most commonly affected site was the hands, with clinically relevant sensitization observed in 15 cases; in 9 of these, the eczema was associated with direct contact with metals, while in 2 cases, hand eczema was linked to exposure to p-phenylenediamine-containing dyes. Analyzing allergic disease prevalence, 50.5% had at least one diagnosed allergic disease as seen in Table I. The total frequency of allergic conditions among the patients was as follows: atopic dermatitis (34.4%), allergic rhinitis (16.2%), and asthma (12.1%). Skin prick test results showed that allergic sensitization was detected in 28% of the patients. The most common sensitization was to pollen, observed in 22.2% of the patients, followed by cat and/or dog allergens in 8.1%, dust mites in 6.1%, and mold in 1.0%.

Patch test positivity was detected in 36/61 females (59%) and 22/38 males (57.9%), with no statistically significant difference between genders ( $p=0.912$ ). Among the 99 patients evaluated in the study, 58 exhibited at least one positive patch test reaction. Of these, 32 patients (55.1%) demonstrated clinically relevant sensitizations, defined by a consistent relationship between the identified allergen, the anatomical site of the lesions, and the documented contact history. These clinically meaningful associations are detailed in Table II.

Allergens were categorized based on their types, with metals comprising the largest proportion at 26.8% of the total positive reactions. Within the metals group, Nickel sulfate (11.8%) was the most frequently detected, followed by Cobalt chloride (5.2%) and Potassium dichromate (2.0%). The Preservatives group accounted for 24% of the reactions, with Methyltribromo glutaronitrile (5.2%), Methylisothiazolinone + Methylchloroisothiazolinone (4.6%) being the most common. Fragrances were responsible for 12% of allergic reactions, with Fragrance mix II (4.6%) and Fragrance mix I (3.3%) being the most common allergens. The Medicaments/Excipients group accounted for 5.5% of reactions, with Neomycin sulfate (2.0%) as the most frequently detected allergen. In the Rubber Additives group (2.8%), Thiuram mix, N-isopropyl-N'-phenyl-4-phenylenediamine, and Mercapto mix each accounted for 0.7%. Resins and Glues (1.8%) had Colophony and Epoxy resin as the primary allergens, each contributing 0.7%. Finally, the Others group, which accounted for 25.9% of reactions, was dominated by Propolis (13.1%), Other allergens with lower frequencies are detailed in Table III.

Patch test positivity was not significantly associated with gender ( $p=0.913$ ), presence of atopic dermatitis ( $p=0.376$ ), age categories (under 12 years and 12 years or older) ( $p=0.221$ ), or presence of other allergic diseases ( $p=0.776$ ). However, a statistically significant difference was found in symptom duration between patients with and without patch test positivity ( $p=0.037$ ). Patients with a

Table II. Allergen Categories, Clinical Presentations, and Associated Positive Patch Test Result

| Category         | Description  | Number of Patients | Associated Positive Allergens   |
|------------------|--|--------------------|---|
| Metals           | Eczema or rash, often triggered by contact with metals           | 20                 | - Nickel (n=14)<br>- Nickel + Cobalt (n=2)<br>- Potassium dichromate + Cobalt (n=1)<br>- Cobalt (n=2)<br>- Potassium dichromate + Cobalt + Nickel (n=1) |
| Fragrances       | Rash associated with perfumes                                    | 2                  | - Fragrance mix I - Lanolin alcohol   |
| Hair Dye         | Rash following hair dye  | 3                  | - Para-phenylenediamine (PPD)   |
| Preservatives    | Rash following use of creams or exposure to automotive batteries | 5                  | - Methylisothiazolinone (MI) and Methylchloroisothiazolinone (MCI) (n=3)<br>- Sesquiterpene lactone mix (n=1)<br>- Formaldehyde (n=1)                   |
| Textile Dye      | Rash associated with socks                                       | 1                  | - Textile dye mix   |
| Rubber Additives | Hand rash due to rubber contact                                  | 1                  | - Thiuram mix   |

Table III. Patch Test Results

| Group                                | Allergen Name                                       | Count | Percentage (%) |
|--------------------------------------|---|-------|----------------|
| <b>Metals (27.1%)</b>                | Nickel sulfate                                      | 18    | 16.8           |
|                                      | Cobalt chloride                                     | 8     | 7.5            |
|                                      | Potassium dichromate                                | 3     | 2.8            |
| <b>Preservatives (24.2%)</b>         | Methyldibromo glutaronitrile                        | 8     | 7.5            |
|                                      | Methylisothiazolinone + Methylchloroisothiazolinone | 7     | 6.5            |
|                                      | Formaldehyde  | 4     | 3.7            |
|                                      | Methylisothiazolinone (0.2%)                        | 4     | 3.7            |
|                                      | Paraben mix   | 2     | 1.9            |
|                                      | Quaternium-15                                       | 1     | 0.9            |
| <b>Fragrances (12.1%)</b>            | Fragrance mix II                                    | 7     | 6.5            |
|                                      | Fragrance mix I                                     | 5     | 4.7            |
|                                      | Myroxylon Pereirae resin (Peru balsam)              | 1     | 0.9            |
| <b>Medicaments/Excipients (5.5%)</b> | Neomycin sulfate                                    | 3     | 2.8            |
|                                      | Benzocaine  | 1     | 0.9            |
|                                      | Lanolin alcohols                                    | 1     | 0.9            |
|                                      | Tixocortol-21-pivalate                              | 1     | 0.9            |
| <b>Rubber Additives (2.7%)</b>       | Thiuram mix   | 1     | 0.9            |
|                                      | N-isopropyl-N'-phenyl-4-phenylenediamine            | 1     | 0.9            |
|                                      | Mercapto mix  | 1     | 0.9            |
| <b>Resins and Glues (1.8%)</b>       | Colophony   | 1     | 0.9            |
|                                      | Epoxy resin   | 1     | 0.9            |
| <b>Others (26.2%)</b>                | Propolis  | 20    | 18.7           |
|                                      | p-Phenylenediamine                                  | 3     | 2.8            |
|                                      | Sesquiterpene lactone mix                           | 2     | 1.9            |
|                                      | Textile dye mix                                     | 3     | 2.8            |
| <b>Total</b>                         |   | 107   | 100.0          |

positive patch test had a shorter mean symptom duration (9.3 months) compared to those with a negative test (14.7 months). No significant associations were found in the risk factor analysis for patch test positivity, including gender, age ( $\geq 12$  years), presence of allergic diseases, presence of atopic dermatitis, and symptom duration ( $\geq 12$  months).

## DISCUSSION

In this study, we evaluated 99 patients with suspected allergic contact dermatitis (ACD), focusing on the demographic characteristics, sensitization patterns, and potential associations with allergic diseases. Patch test positivity was detected in 58 patients (58.6%), among whom 32 (55.1%) had clinically relevant sensitizations, defined by a

consistent correlation between the allergen identified, the anatomical distribution of lesions, and the documented exposure history. When compared with the literature, Boonchai and Lamtharachai reported only the sensitization rates in their study, without further evaluation of clinical relevance (10). Similarly, Pesqué et al. identified occupational exposure in 1% of 513 pediatric patients, but did not explore any association between sensitization and atopy (11). Kalay Yildizhan and Boyvat also reported sensitizations in children, yet atopic status was not evaluated in their analysis (12). In contrast, Lazarov. reported positive patch test results in 937 patients, with clinical relevance determined in 68.4% of the cases (13). No statistically significant difference in sensitization rates was observed between the gen-



ders. Similarly, Lazarov. conducted a study on both pediatric and adult patients, reporting that 937 out of 2,156 individuals (43.5%) had one or more positive allergic patch test reactions (13). In the study by Andre et al., the majority of participants were female (63.8%), and 160 children (43.6%) exhibited at least one positive patch test result (14). Belloni Fortina et al. analyzed data from 6,708 patients, finding that 2,476 (36.9%) had at least one positive reaction to the EBS series. They also reported no significant difference in patch test positivity between genders, although a higher number of female patients were tested (15). Similarly, Acer et al. reported a comparable positivity rate of 57.8% in their study of 135 adult patients, with no significant gender difference in reactions to at least one allergen (16). Finally, in a study focusing on children, Kalay Yıldızhan and Boyvat. found that 49 patients (30.6%) had at least one positive patch test reaction (12).

The most common primary site of dermatitis in our study was the hands (n=44, 44%), followed by the face/head/neck region (n=18, 18%), the trunk (n=15, 15%), and the arms (n=12, 12 %). Similarly, Acer et al. reported that dermatitis most frequently affected the hands (43.7%), followed by the trunk (27.4%) and the face (19.3%) (16). In a study by Zug et al., pediatric ACD was most commonly observed on the face, in a generalized scattered distribution pattern, and on the extremities (arms and legs) (17). Likewise, Lazarov. identified the hands (30.7%), face and neck (23.9%), and extremities (11.3%) as the most frequently affected sites (13). In a study involving adult patients by Koca et al. the localization of dermatitis was found to be predominantly on the hands (69.7%), followed by the feet (22.8%), face (19.4%), and body (20.4%). Notably, 499 patients (42.7%) had only hand involvement (18). These findings underscore the variation in dermatitis localization across different studies, with hands consistently emerging as the most commonly affected site (11).

The total frequency of allergic conditions among the patients was as follows: AD (34.4%), allergic rhinitis (16.2%), and asthma (12.1%). Similarly, Kalay Yıldızhan and Boyvat, reported that 68 patients (42.5%) had a history of atopy, with AD diagnosed in 36 patients (22.5%) (12). Lazarov found that atopy and asthma were present in 472 patients (21.9%), including 205 (9.5%) with AD, 237 (11.0%) with mucosal atopy and/or asthma, and 30 (1.4%) with both conditions (13). In the study by Koca et al., 291 (24.9%) of the 1169 patients tested were designated as "atopic".

Among the atopic patients, 103 had allergic rhinitis (8.8%), 44 had asthma (3.8%), and 48 had AD (4.1%)(18).

Allergens were categorized by type, with metals being the most common and accounting for 26.8% of positive reactions, followed by preservatives (24.0%), and others (25.9%). Among metal allergens, nickel sulfate (11.8%), cobalt chloride (5.2%), and potassium dichromate (2.0%) were the most frequently detected. Similarly, Acer et al. identified the most common allergens as nickel sulfate (27.4%), potassium dichromate (14.8%), cobalt chloride (11.9%), and textile dye mix (8.1%) (16). According to Belloni Fortina et al., the most common allergens were nickel sulfate (16.7%), cobalt chloride (7.5%), potassium dichromate (5.2%), and neomycin sulfate (3.2%) (15). Lazarov et al. reported nickel sulfate (13.9%) as the most frequent contact allergen, followed by fragrance mix (7.1%), potassium dichromate (3.8%), and Balsam of Peru (3.6%) (13). Kalay Yıldızhan and Boyvat, found that metals were the most prevalent allergen group (13.8%), followed by preservatives (10%), dyes (6.2%), and fragrances (4.4%)(12). Their five most common allergens were nickel sulfate (10.6%), Methylchloroisothiazolinone (MCI) / Methylisothiazolinone (MI) (8.1%), cobalt chloride (5.6%), p-phenylenediamine (PPD) (5%), and MI (3.5%). In our study, the most frequently detected allergen was propolis, and there are also studies in the literature reporting propolis as the most common allergen (19). We believe the high prevalence of propolis allergy in our study is due to its widespread use in natural products, particularly in oral health products, honey-based formulations, and skincare products. Our study supports the existing literature by demonstrating that metals and preservatives are the most frequent triggers of ACD (11, 20).

### Limitations

This study has several limitations that should be acknowledged. First, its retrospective design inherently restricts the ability to establish causal relationships and may not account for all potential variables influencing sensitization rates. Second, the absence of a detailed exposure history limited our capacity to identify specific sources of allergen exposure. This is particularly relevant for substances like propolis, which may be present in a variety of health-related products, including dietary supplements and topical formulations, and these were not systematically recorded. Finally, the inability to pinpoint precise

sources of allergen exposure may have contributed to the high frequency of propolis sensitization observed in our cohort. These limitations should be considered when interpreting the findings. Future prospective studies with more rigorous tracking of exposure history and allergen sources are warranted to address these gaps.

## CONCLUSION

Studies have shown that ACD occurs in the pediatric age group at rates similar to those observed in adults. Infants and young children are exposed to a wide range of foreign substances through various sources, including diet, clothing, toys, and hygiene products, as they grow. This continuous exposure increases the risk of developing allergic sensitization. Given its impact on the quality of life and potential chronicity, ACD represents a significant health concern in the pediatric population, highlighting the need for early diagnosis and preventive measures.

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## Conflict of Interest

The authors declare that they have no conflict of interest.

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## Author Contributions

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