

Allergic contact dermatitis in patients with atopic dermatitis: A retrospective study

Maddalena Napolitano, MD^a, Gabriella Fabbrocini, MD^b, and Cataldo Patruno, MD, PhD^c



Clinical Implications

- The relationship between atopic dermatitis (AD) and allergic contact dermatitis is not clear. Patch testing should be considered in patients with AD, especially when AD does not respond to or worsens with topical therapy. The rate of contact sensitization seems to be higher in adults with persistent disease, probably due to long exposure of a large number of topical products.

TO THE EDITOR:

Atopic dermatitis (AD) is a chronic, recurrent, inflammatory skin disease that predominantly affects children. However, it can persist in adulthood or have a later onset.¹ AD is associated with skin barrier disruption, increased skin absorption of irritants, and contact allergens.

AD therapies involve the use of topical emollients and medications, many of which might contain known contact sensitizers.² For this reason, it has been hypothesized that the risk for allergic contact dermatitis (ACD) is higher in patients with AD. The relationship between the pathogenesis of these 2 diseases is complex and their association debated.³ Indeed, some authors found no specific associations between ACD and atopy, whereas others revealed a significant difference in sensitization in atopic versus nonatopic patients.⁴ A recent review confirmed ACD to be clinically significant in patients with AD.³ In this study, we sought to evaluate the frequency of cutaneous sensitization in both children and adult patients with AD and identify the most frequent causative allergens. We performed a retrospective evaluation of consecutive patients who were referred to the Dermatology Unit of the University of Naples Federico II from January 2008 to June 2018 for patch testing. They all were affected by eczema, which we suspect was caused or possibly worsened by allergic contact sensitization. A total of 11,022 patients (5,712 males, 51.8%; mean age, 49.2 ± 15.2 years) were patch tested after a detailed history and clinical examination performed by a dermatologist (C.P.). They all signed an informed consent. All patients were tested with the SIDAPA (Società Italiana di Dermatologia Allergologica Professionale e Ambientale) baseline series in use at the time of testing. Because the series is periodically reviewed, some allergens were not tested in all the patients (Table I). Furthermore, expanded series were performed in 2,711 of 11,022 (24.6%) patients, based on medical history and results of baseline series. The test was performed according to guidelines in use at the time of testing.^{5,6} The reading was done at day (D) 2 and D4; at D7 in doubtful case. Positive patch test result was classified as +/++/+++ according to the intensity of reaction. False-positive

(irritant) reactions were also registered. Diagnosis of AD was made in 963 of 11,022 patients (8.7%), using Hanifin and Rajka criteria⁷ (617 of 963 [64.1%]) or based on the anamnesis for patients without ongoing clinical features (346 of 963 [35.9%]). The AD group consisted of 463 adults (48.1%) and 500 pediatric patients (<18 years old [51.9%]); 495 (51.4%) were males. The mean age was 29.2 ± 8.3 years. Adult-onset AD was noted in 39.9% of patients (185 of 463). No significant differences regarding the number of patients positive to patch test were found between patients with AD and patients who were diagnosed with eczema other than AD (other diagnosis [OD] group) (339 of 963 [35.2%] vs 3,712 of 10,059 [36.9%]; $P = 0.7$). As far as positive patients of both groups are concerned, polysensitization occurred in 74 (21.8%) patients with AD and in 683 (18.4%) patients in the OD group ($P = .4$). A total of 438 positive and 102 irritant reactions were found in patients with AD. Instead, in the OD group, 4810 positive reactions and 789 irritant reactions were found. Irritant reactions were mainly due to cobalt chloride, 46.1% in patients with AD and 33.1% in patients in the OD group. Disperse dye mix was also a frequent irritant; irritant reactions were found in 208 of 699 (29.8%) cases (39 of 119 [32.8%] patients with AD and 169 of 580 [29.1%] patients in the OD group). Nickel sulfate was the main sensitizer in both groups, with positive patch test result in 128 of 438 (29.2%) patients with AD and 1521 of 4810 (31.6%) patients in the OD group. In the OD group, nickel sulfate was followed by *P*-phenylenediamine (1019 of 4810 [21.2%]) and potassium dichromate (432 of 4810 [9.0%]). In the AD group, the other main sensitizers were fragrances (balsam of Peru, fragrance mix I, fragrance mix I/ sorbitan sesquileate, fragrance mix II, and Lyrall) (97 of 438 [22.1%]) followed by isothiazolinones (Kathon CG 0.01% or 0.02%, and methylisothiazolinone) (73 of 438 [16.7%]), and corticosteroids (budesonide, hydrocortisone-21-acetate, desoxymethasone, and corticosteroid mix) (49 of 438 [11.2%]). The sum of reactions toward these positive patch test allergens (commonly found in products for topical use) was 219 of 438, thereby being 50.0% of all the positive patch test results found in patients with AD. Nine of 339 (2.7%) patients had a positive patch test result to 1 of their topical personal products. In all of them, there was a history of worsening of the disease after the application of that product, and patch test result with baseline and additional series was negative. The products were tested following the current guidelines on patch testing.^{5,6} This feature was found in 28 of 3712 (0.8%) patients in the OD group. As far as childhood or adult AD is concerned, the number of positive adult patients was higher to that found in the children group (204 of 463 [44.1%] vs 135 of 500 [27.1%]; $P = .3$), but there were no significant differences in the frequency of allergens. There was a higher percentage of positive patients with persistent AD (142 of 278 [51.1%]) among adults with AD than with adult-onset AD (62 of 185 [33.5%]).

The relationship between AD and ACD has long been debated in literature, with conflicting results.³ This is mainly due to differences in pathogenesis between these 2 diseases. AD is a T_H2 -driven inflammatory response secondary to disruption of skin barrier, whereas ACD is a delayed hypersensitivity reaction after contact with a specific allergen. Some authors⁸ reported that

TABLE I. Allergens tested with SIDAPA baseline series from January 2008 to June 2018

Allergen	No. of total patients tested	No. of patients with AD tested (%)	No. of positive patch test results (% of total tested patients)
Balsam of Peru 25% pet	11,022	963 (8.7)	96 (0.9)
Benzocaine 5% pet	11,022	963	7 (0.1)
Cobalt chloride 1% pet	11,022	963	155 (1.4)
Colophony 20% pet	11,022	963	82 (0.7)
Epoxy resin 1% pet	11,022	963	38 (0.3)
Lyrar 2% pet	11,022	963	42 (0.4)
Mercapto mix 2% pet	11,022	963	63 (0.6)
Mercaptobenzothiazole 2% pet	11,022	963	72 (0.7)
Neomicine sulfate 20% pet	11,022	963	6 (0.1%)
Nickel sulfate 5% pet	11,022	963	1,649 (15.0)
<i>P</i> -Phenilendiamine 1% pet	11,022	963	1,061 (9.6%)
<i>P-Tert</i> -butylphenol-formaldehyde resin 1% pet	11,022	963	43 (0.4)
Paraben mix 16% pet	11,022	963	19 (0.2)
Phenylisopropyl <i>P</i> -phenilendiamine 0.1% pet	11,022	963	81 (0.8)
Potassium dichromate 0.5% pet	11,022	963	447 (4.1%)
Thiram mix 1% pet	11,022	963	103 (0.9)
Wool alcohol 30% pet	11,022	963	62 (0.6)
Dibromodicyanobutane 0.3% pet	10,442	498 (4.8)	76 (0.7)
Disperse blue 124 1% pet	10,442	498	128 (1.2)
Formaldehyde 1% aq	10,442	498	57 (0.5)
Kathon CG 0.01% aq	10,442	498	264 (2.5%)
Budesonide 0.01% pet	6,839	456	92 (1.3)
Fragrance mix I/Sorbitan sesquileate 5% pet	6,839	456	181 (2.6)
Fragrance mix II 14% pet	6,839	456	95 (1.4)
Hydrocortison 21-acetate 1% pet	6,839	456	58 (0.8)
Corticosteroid mix 3.1% pet	4,183	161 (3.8)	31 (0.7)
Desoximethasone 1% pet	4,183	161	27 (0.6)
Disperse yellow 3 1% pet	4,183	161	29 (0.7)
Fragrance mix I 8% pet	4,183	61	97 (1.5)
Dimethylaminepropylamine 1% aq	580	119 (20.6)	6 (1.3)
Disperse dye mix 6.6% pet	580	119	5 (0.9)
Formaldehyde 2% aq	580	119	8 (1.4)
Idrossiethyl methacrilate 2% pet	580	119	13 (2.2)
Kathon CG 0.02% aq	580	119	39 (6.7)
Methylisothiazolinone 0.2% aq	580	119	13 (2.2)
Sorbitan sesquileate 20% pet	580	119	3 (0.5)

aq, In water; pet, in petrolatum.

patients with AD were less prone to develop delayed contact sensitization caused by the impairment of epidermis and delayed immune response. Other authors have reported that patients with AD can develop ACD when they use topical products for dermatitis.² Our data seem to suggest that the rate of contact sensitization in patients with AD does not differ from that of other eczematous conditions. However, contact allergy may be considered as one of the most important comorbidities of AD.⁹ We confirm that allergens contained in topical preparations are the main sensitizers. This is especially true in adult AD with persistent disease, probably because of the prolonged exposure to a large number of topical products. The suspicion of contact sensitization must arise especially for patients who do not improve or worsen with potentially beneficial topical treatments. Therefore, all these patients

should be patch tested. Moreover, the disrupted epidermis in AD may help the penetration of allergens into the skin. Patch test is the criterion standard for the diagnosis of ACD, even if it requires some adjustments in patients with AD.³ The individual with AD has a low irritancy threshold; therefore, false-positive reactions are often registered as found in our AD group. In our experience, it has not always been possible to detect these allergies using available series of allergens. Then, at least in selected cases, topical products should be tested as well. However, some differences exist among our data and those reported by Rastogi et al,² mainly regarding the frequency of positivity to some allergens, namely, lanolin, neomycin, and chlorhexidine. This is likely the result of a different territorial availability of topical preparations and of a different prescriptive habit between the United States and Italy.

^aDepartment of Medicine and Health Sciences Vincenzo Tiberio, University of Molise, Campobasso, Italy

^bSection of Dermatology, Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy

^cDepartment of Health Sciences, University of Catanzaro "Magna Graecia," Catanzaro, Italy

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication November 21, 2018; revised March 26, 2019; accepted for publication March 26, 2019.

Available online April 5, 2019.

Corresponding author: Maddalena Napolitano, MD, Department of Medicine and Health Sciences, Vincenzo Tiberio, University of Molise, Campobasso, Italy.

E-mail: maddy.napolitano@gmail.com.

2213-2198

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<https://doi.org/10.1016/j.jaip.2019.03.045>

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