

Atopy Associated With Positive Patch Test and Possible Allergic Contact Dermatitis

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Canadian
Dermatology
AssociationAssociation
canadienne de
dermatologieMark G. Kirchhof¹ and Gillian C. de Gannes^{2,3}

Abstract

Background: Atopy is a genetic predisposition to the development of allergic reactions and the increased production of immunoglobulin E (IgE) upon exposure to environmental antigens. Clinical manifestations of atopy include asthma, atopic dermatitis (AD), and allergic rhinoconjunctivitis (ARC).

Objective: To determine if cutaneous delayed hypersensitivity reactions (CDHRs) as assessed by patch testing are higher among patients with a history of atopy and with a familial predisposition to atopy.

Methods: For this study, we reviewed the patch test database of the UBC Contact Dermatitis Clinic over a 4-year time span. A personal history of asthma, AD, and ARC was recorded. In addition, a family history was obtained and manifestations of atopy in family members were noted.

Results: A total of 1515 patients were included in this study. Our data show that the odds ratio (OR) of a positive patch test with a personal history of atopy was 1.39, while the OR of a positive patch test with a family history of atopy was 1.69. Conversely, a personal history of respiratory atopy did not significantly affect the probability of a positive patch test, with an OR of 1.03.

Conclusion: We conclude from our study that patients with a personal or family history of atopy have an increased risk of allergic contact dermatitis (ACD). These results provide further evidence for the link between atopy and ACD and suggest that children of atopic parents should avoid potential contact allergens and would likely benefit from prophylactic emollient use.

Keywords

allergic contact dermatitis, atopy, atopic dermatitis, atopic triad, cutaneous delayed hypersensitivity reaction

Atopy is a genetic predisposition to the development of allergic reactions to environmental stimuli and manifests clinically as allergic rhinoconjunctivitis (ARC), allergic asthma, and atopic dermatitis (AD). The skin of atopic individuals is often characterized by immune hyperreactivity and a disruption of the epidermal barrier. This predisposes atopic skin to increased reactions and access to irritants, microbes, and allergens. Allergic contact dermatitis or contact hypersensitivity is a T-cell-mediated immune response facilitated by haptens in sensitized individuals.¹ The result is that individuals with contact hypersensitivity are more likely to react to contact allergens, developing pruritic erythematous edematous papules or plaques that can evolve in severity to include vesiculation and systemic symptoms.

The link between atopy and contact hypersensitivity is controversial. Several reports suggest that individuals with AD have an increase in the likelihood of contact hypersensitivity, while others refute this link.²⁻⁵ Furthermore, some studies use atopy and atopic dermatitis synonymously, making the analysis of results more difficult. In one epidemiologic study,

analysis of patients with occupational allergic contact dermatitis (ACD) revealed that 60% were atopic compared with a prevalence of 30% atopy in the general population.⁶ Allergic contact dermatitis and AD have been more extensively studied. In one recent large analysis of results from patch testing in the United States, patients with AD were statistically more likely to have a positive patch test result compared with patients without AD.⁴ Several authors have suggested that patients with AD should avoid contact with fragrances,

¹Division of Dermatology, Department of Medicine, University of Ottawa and The Ottawa Hospital, Ottawa, ON, Canada

²Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC, Canada

³Division of Dermatology, Department of Medicine, St. Paul's Hospital, Vancouver, BC, Canada

Corresponding Author:

Mark Kirchhof, Division of Dermatology, Department of Medicine, University of Ottawa and The Ottawa Hospital, 737 Parkdale Ave, Ottawa, ON K1Y 4E9, Canada.

Email: mkirchhof@toh.ca

Table 1. Prevalence of Positive Patch Tests Related to Atopic Triad.

Characteristic	Positive Patch Test, % (No.)	Negative Patch Test, % (No.)
All (N = 1515)	66.7 (1011)	33.3 (504)
No atopy (n = 863)	63.6 (549)	36.4 (314)
ARC (n = 225)	71.6 (161)	28.4 (64)
Asthma (n = 49)	67.3 (33)	32.7 (16)
Atopic dermatitis (n = 112)	79.5 (89)	20.5 (23)
ARC, asthma (n = 89)	56.2 (50)	43.8 (39)
ARC, AD (n = 82)	75.6 (62)	24.4 (20)
Asthma, AD (n = 24)	70.8 (17)	29.2 (7)
ARC, Asthma, AD (n = 71)	70.4 (50)	29.6 (21)

AD, atopic dermatitis; ARC, allergic rhinoconjunctivitis.

metals, and getting tattoos due to the increased likelihood of developing a contact hypersensitivity.^{4,7,8}

In this study, we sought to determine the link between a positive patch test result or contact hypersensitivity and atopy. While the previously mentioned publication showed a predisposition to a positive patch test and AD, there has been no similar study examining atopy and the atopic triad. This is particularly important given the controversies of linking AD and ACD. The analysis of patients with asthma and ARC may help better illustrate if atopic disease predisposes patients to a positive patch test result, in the absence of a history of AD. Furthermore, we look at a genetic predisposition or a family history of atopy as another method to better clarify the link between atopy and contact hypersensitivity without a personal history of AD that might cloud the results. This information will be of particular importance for clinicians counselling patients with atopy or a family history of atopy when trying to prevent the development of possible contact sensitizations.

Methods

Patients presenting to the UBC Contact Dermatitis Clinic from January 2008 to December 2012 for evaluation of possible ACD were included in this study. Patients were patch tested using the North American Contact Dermatitis Group (NACDG) screening allergen series. Before undergoing patch testing, patients completed a questionnaire that gathered demographic information; possible location of ACD; personal history of AD, asthma, and ARC; and a family history of atopy (AD, asthma, ARC). The diagnosis of AD was made empirically based on questioning by the clinician using the criteria proposed by Hanifin and Rajka.⁹ A diagnosis of ARC was similarly based on empirical questioning regarding symptoms of nasal congestion, sneezing, and conjunctivitis related to contact with a possible allergen. A diagnosis of asthma was usually determined by questioning the patient about his or her medical history and medications, such as “puffers,” that had been prescribed previously.

Patch testing for the NACDG allergen series (Chemotechnique Diagnostics, Vellinge, Sweden; SmartPractice Canada, Calgary, Alberta, Canada) was performed using IQ-Ultra chambers (Chemotechnique Diagnostics) applied to the upper back with Scanpor tape (Norgesplaster, Vennesla, Norway). The initial reading was done at 48 hours, while delayed readings were taken at 96 to 120 hours. Patch test reactions were interpreted using the International Contact Dermatitis Research Group (ICDRG) scale, with 1+, 2+, and 3+ considered a positive reaction.

Patients included in this study signed a consent form agreeing to have their deidentified information included in the UBC Contact Dermatitis computer database (Excel 2010; Microsoft Corp, Seattle, Washington) to be used for research and study purposes. Since only deidentified data with appropriate patient consent were used, this study was considered exempt from institutional review board approval at the University of British Columbia.

The presence of a positive or negative patch test result was correlated with ARC, asthma, AD, and a family history positive for any of the atopic triad. Results were grouped by patients who had evidence of atopic skin disease alone (AD), patients who only had respiratory atopic disease (ARC, asthma), patients who had any of the atopic triad (ARC, AD, asthma), and those who had a positive family history of atopy. Odds ratios (ORs) were calculated with 95% confidence intervals (CIs).

Results

A total of 1515 patients were patch tested from 2008 to 2012, with 66.7% of those patients having at least one positive patch test result (Table 1). These patients were presenting to the clinic for evaluation of a possible ACD. The prevalence of each of the manifestations of the atopic triad was noted, with 225 patients having ARC alone, 29 having asthma alone, and 112 having AD alone. Combinations of ARC, asthma, and AD were also noted. Of the 1515 patients, 89 had asthma and ARC, 82 had ARC and AD, 24 had AD and asthma, and 71 had all 3 components of the atopic triad. For each of these identified categories, the prevalence of a positive or negative patch test was noted. Patients with AD alone had the highest prevalence of a positive patch result at 79.5% while patients with ARC and asthma had the lowest prevalence of a positive patch test result at 56.2%.

Patients were then grouped, and the total number of patients with positive and negative patch tests for each group was determined (Table 2). Of the patients who had a personal history of any of the atopic triad, 70.9% had a positive patch test compared with patients who had no history of any of the atopic triad, of whom only 63.6% had a positive patch test. When only patients with a personal history of AD were evaluated, 75.4% had a positive patch test compared with 64.8% of patients who did not have a personal history of AD. Patients who only had respiratory symptoms of atopy (asthma and ARC) had a prevalence of a positive patch test of 67.2%,

Table 2. Prevalence of Positive Patch Tests for Atopy, Atopic Dermatitis, Respiratory Atopy, and Family History of Atopy.

Characteristic	Positive Patch Test, % (No.)	Negative Patch Test, % (No.)
Personal history of atopic triad (asthma, ARC, or AD)		
Yes (n = 652)	70.9 (462)	29.1 (190)
No (n = 863)	63.6 (549)	36.4 (314)
Personal history of AD		
Yes (n = 289)	75.4 (218)	24.6 (71)
No (n = 1226)	64.8 (794)	35.2 (433)
Personal history of respiratory atopy (asthma and ARC)		
Yes (n = 363)	67.2 (244)	32.8 (119)
No (n = 1152)	66.6 (767)	33.4 (385)
Family history of atopic triad (asthma, ARC, or AD)		
Yes (n = 630)	73.3 (462)	26.7 (168)
No (n = 885)	62.0 (549)	38.0 (336)

AD, atopic dermatitis; ARC, allergic rhinoconjunctivitis.

Table 3. Odds Ratio of a Positive Patch Test Result.

Characteristic	Odds Ratio (95% Confidence Interval)
Personal history of atopy	1.39 (1.12-1.73)
Personal history of atopic dermatitis	1.67 (1.25-2.24)
Personal history of respiratory atopy (asthma-ARC) with no skin disease	1.03 (0.80,1.32)
Family history of atopy	1.69 (1.35-2.11)

ARC, allergic rhinoconjunctivitis.

which was similar to the 66.6% prevalence of a positive patch test for patients who had no history of respiratory symptoms of atopy. Finally, 73.3% of patients with a family history of atopy had a positive patch test compared with 62.0% for those who had no family history of atopy.

With the prevalence of positive and negative patch tests determined for each group (Table 2), the OR and 95% CI were calculated (Table 3). The OR for a positive patch in a patient with a history of atopy was 1.39 with a 95% CI of 1.12 to 1.73. Since the 95% CI does not cross 1.0, this is considered a significant result and indicates that patients with a personal history of atopy are more likely to have a positive patch test result. The OR was even higher for patients with a personal history of AD (1.67; 95% CI, 1.25-2.24) and family history of atopy (1.69; 95% CI, 1.35-2.11). This suggests that a personal history of AD or a family history of atopy is stronger risk factor for a positive patch test than a personal history of atopy. Conversely, a personal history of respiratory symptoms of atopy (ARC, asthma) did not significantly affect the probability of a positive patch test, with an OR of 1.03 and a 95% CI that crossed 1.0 (0.80-1.32).

The patient-described location of the ACD in relation to the atopic history of the patient was assessed (Table 4). Overall, there was a similar distribution of anatomical locations of possible ACD between patients who had a history of atopy and those who did not. However, atopic patients had a higher prevalence of possible ACD of the hands (36.8%), face (28.2%), and eyelids (15.6%). The prevalence of hand ACD was also noted to be even higher among patients with AD alone (40.2%), ACR with AD (41.5%), and patients with ACR, AD, and asthma (49.3%). The other noteworthy finding was that patients with asthma alone had possible ACD affecting the body (24.5%) and arms (22.4%) at rates twice as high as the average for the entire study group.

Discussion

The association between atopy and ACD remains controversial. Several studies have shown that patients with AD have a lower incidence of ACD and cutaneous hypersensitivity reactions.¹⁰⁻¹² However, several recent studies and reviews of the literature have supported the association between AD and ACD.^{4,7,13,14} In this study, we show not only that AD is associated with a positive patch test result but also that atopy in general and a family history of atopy are associated with an increased incidence of a positive patch test and possible ACD. Interestingly, a personal history of respiratory symptoms of atopy (asthma and ARC) is not associated with a positive patch test. These data support the association of atopic skin disease and a genetic predisposition with a positive patch test and possible ACD.

The relationship between ACD and AD can be justified based on the principle of sensitization to contact allergens in individuals prone toward barrier dysfunction of the skin. One of the most common mutations associated with AD is a filaggrin loss-of-function mutation.^{15,16} Filaggrin is a key protein in the formation of the outermost layer of the epidermis, known as the stratum corneum. Filaggrin aggregates keratin filaments, aiding in the formation of a protein and lipid barrier that is important in skin function. When filaggrin function is lost, there is an increase in transepidermal water loss as well as increased permeability to microbes, irritants, and potential allergens.¹⁷⁻¹⁹ It follows that filaggrin loss-of-function mutations result in an increased potential for the development of ACD.^{20,21} The risk of ACD in patients with filaggrin mutations is particularly high if there is a history of dermatitis, suggesting that a filaggrin mutation alone is not enough to promote ACD development.²⁰ The development of ACD also likely requires an immunologically potentiated environment. It is known that atopic patients have increased levels of Th2 cytokines.²²⁻²⁵ Some of these cytokines may promote inflammation, pruritus, and the development of ACD.^{22,26,27} Apart from cytokines, it seems that the antigen presentation and processing components of the immune system are also elevated in atopic patients.^{28,29} This potentiates atopic patients to antigen- or allergen-driven immune activation. Exposure to irritants

Table 4. Patient-Identified Location of Possible Allergic Contact Dermatitis.

Anatomical Location of Patients, % (No.)														
Patient Category	Hands	Face	Eyelids	Lips	Scalp	Neck	Body	Arms	Back	Chest	Legs	Feet	Other	Not Specified
All (N = 1515)	33.1 (501)	25.6 (388)	12.7 (193)	5.4 (82)	6.1 (93)	10.0 (152)	13.3 (201)	12.7 (193)	5.1 (78)	2.8 (42)	10.2 (154)	6.3 (96)	3.3 (50)	6.6 (100)
No atopy (n = 863)	30.2 (261)	23.6 (204)	10.5 (91)	5.1 (44)	5.9 (51)	9.4 (81)	14.0 (121)	13.2 (114)	4.8 (41)	2.3 (20)	10.5 (91)	7.2 (62)	4.9 (42)	7.4 (64)
Atopy (n = 652)	36.8 (240)	28.2 (184)	15.6 (102)	5.8 (38)	6.4 (42)	10.9 (71)	12.3 (80)	12.1 (79)	5.7 (37)	3.4 (22)	9.7 (63)	5.2 (34)	1.2 (8)	5.5 (36)
ARC (n = 225)	35.1 (79)	23.6 (53)	19.6 (44)	4.4 (10)	5.3 (12)	11.1 (25)	12.0 (27)	18.7 (42)	7.6 (17)	4.0 (9)	14.2 (32)	4.4 (10)	1.3 (3)	5.3 (12)
Asthma (n = 49)	28.6 (14)	32.7 (16)	12.3 (6)	4.1 (2)	4.1 (2)	10.2 (5)	24.5 (12)	22.4 (11)	6.1 (3)	4.1 (2)	12.2 (6)	8.2 (4)	0.0 (0)	4.1 (2)
Atopic dermatitis (n = 112)	40.2 (45)	26.8 (30)	15.2 (17)	8.0 (9)	8.9 (10)	8.9 (10)	11.6 (13)	8.9 (10)	4.5 (5)	1.0 (1)	8.0 (9)	7.1 (8)	1.8 (2)	2.7 (3)
ARC, asthma (n = 89)	29.2 (26)	28.1 (25)	14.6 (13)	2.2 (2)	10.1 (9)	11.2 (10)	10.1 (9)	7.9 (7)	5.6 (5)	6.7 (6)	5.6 (5)	4.5 (4)	2.2 (2)	10.1 (9)
ARC, AD (n = 82)	41.5 (34)	34.1 (28)	14.6 (12)	12.2 (10)	4.9 (4)	12.2 (10)	6.1 (5)	3.7 (3)	4.9 (4)	2.4 (2)	6.1 (5)	2.4 (2)	1.2 (1)	6.1 (5)
Asthma, AD (n = 24)	29.2 (7)	33.3 (8)	20.8 (5)	4.1 (1)	12.5 (3)	12.5 (3)	12.5 (3)	8.3 (2)	0.0 (0)	4.1 (1)	12.5 (3)	0.0 (0)	0.0 (0)	8.3 (2)
ARC, asthma, AD (n = 71)	49.3 (35)	33.8 (24)	7.0 (5)	5.6 (4)	2.8 (2)	11.3 (8)	15.5 (11)	5.6 (4)	4.2 (3)	1.4 (1)	4.2 (3)	8.5 (6)	0.0 (0)	4.2 (3)

AD, atopic dermatitis; ARC, allergic rhinoconjunctivitis.

and a history of irritant dermatitis may also factor into the development of ACD. Irritants may cause breakdown of the skin barrier, allowing allergens to interact with the immune system of the skin. When patch test sites are pretreated with an irritant, there is an increased chance of developing an ACD reaction, and the concentration of allergen required to elicit a positive test is decreased.³⁰⁻³³ Finally, it is known that atopic individuals who have AD are more likely to be applying numerous products to their skin.^{34,35} This increased exposure may sensitize atopic patients to allergens and the development of ACD. Indeed, our findings that the hands, face, and eyelids were the most common sites for possible ACD in atopic patients corroborates the role of increased allergen exposure in the pathogenesis of ACD. The hands, face, and eyelids are the most common sites to which people apply topical products like makeup, cleansers, and emollients.

While this study aimed to address the connections between atopy and more specifically the atopic triad and ACD, previous studies largely focused on the association of ACD with AD. The association of AD with ACD has been controversial at times. Patients with AD were thought to have a lower likelihood of developing ACD based on studies that showed that sensitization to a contact allergen occurred less in patients with AD compared with controls.^{10,11,36} These studies used dinitrochlorobenzene to induce an ACD experimentally. The results were that patients with AD developed less ACD and that the more severe the AD, the less likely it was that the patient would develop a reaction to dinitrochlorobenzene.^{10,11,36} However, numerous studies have now demonstrated that ACD occurs as often if not more often in patients with AD.^{4,7,13,14} Furthermore, the duration, extent, and severity of AD seem to correlate with a greater propensity to ACD development, reinforcing the potential for shared pathogenesis.^{3,4,35} Our data confirm and extend the link between AD and ACD.

Not only did we note an increased risk of ACD with AD but also found that a family history of atopy correlated with ACD. This suggests that there is a strong genetic component to barrier dysfunction and immune dysregulation. We know that when both parents are atopic, there is a 70% chance that their children will have manifestations of atopy.³⁷⁻³⁹ Since we know that children of atopic parents also have an increased risk of ACD development, it follows that avoidance of some of the common contact allergens might be prudent in this population. The use of products that contain little to no preservatives and are fragrance and dye free should be advised for all atopic parents of newborns. Metals such as nickel and cobalt are also common contact allergens that should be avoided in newborns from atopic parents.⁴ Studies show that liberal and repeated emollient use in newborns who are predisposed to AD might be able prevent the development of AD or limit the severity of disease.^{40,41} Based on these findings, it is quite plausible that the use of emollients may also limit access of contact allergens to the skin and prevent the development of ACD in individuals with an atopic family history.

While this retrospective chart review provides clear statistically significant evidence linking atopy and positive patch test results, there are several limitations to this study. The reporting of atopic symptoms and a family history of atopy is based on self-reported patient information. Particularly, a history of AD might be confused and complicated by a possible diagnosis of ACD. This also follows from the strong association with a positive patch test and a personal history of AD. However, the strong correlation between a family history of atopy and a positive patch test bypasses the potential difficulties in separating ACD from AD. Another important consideration in the interpretation of the data is that no clinical correlation between a positive patch and a relevant ACD is made. It is for this reason that the associations reported in this study are between atopy and a positive patch test result, which suggest but do not confirm a relationship between atopy and ACD. Follow-up to determine if avoidance of specific allergens results in resolution of ACD would be needed.

Conclusion

Based on the data from the patch test database of the UBC Contact Dermatitis Clinic over a 4-year time span, we showed that a personal history of atopy or AD or a family history of atopy is associated with an increased likelihood of having a positive patch test result and likely ACD. Interestingly, a personal history of asthma or ARC did not correlate with a positive patch test result, suggesting that respiratory symptoms of atopy were not predisposing factors to ACD. It seems that the most important factors needed to develop ACD were a genetic predisposition and cutaneous sensitization. Our data suggest that children of atopic parents should avoid potential contact allergens and would likely benefit from prophylactic emollients to limit cutaneous sensitization.

Declaration of Conflicting Interests

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