

Eczematous Skin Reaction to Atopy Patch Testing With Cockroach in Patients With Atopic Dermatitis

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■ Abstract

Background: Aeroallergens from house dust mite (HDM) may be an important trigger in a subgroup of patients with atopic dermatitis (AD). HDM and cockroach (CR) contain cross-reactive allergens, such as tropomyosin.

Objective: To investigate the diagnostic value of patch testing with an aeroallergen and the role of CR allergen and HDM allergen in persons with AD.

Methods: We performed skin prick tests (SPT) with a panel of common aeroallergens and total serum immunoglobulin (Ig)E and specific IgE tests for CR and HDM on 23 patients with AD and 9 nonatopic control participants. Atopy patch tests (APT) were performed with CR and HDM extracts on clinically uninvolved skin on the back, and evaluated after 48 and 72 hours.

Results: A positive APT reaction to CR was found in 10/23 (43%) patients with AD. No positive reactions were observed in the nonatopic control participants. Positive APT reactions for CR showed no significant correlation with SPT or specific IgE levels for this allergen. Twelve of the 23 (52%) patients with AD were also sensitized to HDM. There was no significant correlation between positive results for SPT, APT, and specific IgE to CR and HDM.

Conclusion: We demonstrate that CR allergens can induce positive patch test reactions in patients with AD. The absence of a significant correlation to SPT and specific IgE antibodies suggests that T-cell- and IgE-sensitization may be mediated by different allergens. There was no significant relationship between CR and HDM sensitivity, thus indicating no major cross-reactivity.

Key words: Atopic dermatitis. Atopy patch test. Cockroach. Cross-reactivity to house dust mite.

■ Resumen

Antecedentes: Los aeroalérgenos procedentes de los ácaros del polvo doméstico (APD) pueden ser importantes desencadenantes en un subgrupo de pacientes con dermatitis atópica (DA). Los APD y las cucarachas (CR) contienen alérgenos con reactividad cruzada, como la tropomiosina.

Objetivo: Investigar el valor diagnóstico de la prueba epicutánea con aeroalérgenos y el papel del alérgeno CR y del alérgeno APD en personas con DA.

Métodos: Realizamos pruebas cutáneas del prick (PCP) con un panel de alérgenos inhalantes comunes, e IgE total sérica e IgE específica para CR y APD en 23 pacientes con DA y 9 sujetos controles no atópicos. Se realizaron pruebas epicutáneas (PE) con extractos de CR y en piel no afectada clínicamente de la espalda, y evaluó tras 48 y 72 horas.

Resultados: Se encontró reacción positiva de la PE a CR en 10/23 (43%) pacientes con DA. No se observaron reacciones positivas en los participantes controles no atópicos. Las reacciones positivas de PE para CR mostraron una correlación no significativa con las PCP o los niveles de IgE específica para este alérgeno. Doce de los 23 (52%) pacientes con DA estaban también sensibilizados a APD. No había correlación significativa entre los resultados positivos para PCP, PE, e IgE específica a CR y APD.

Conclusión: Demostramos que los alérgenos CR pueden inducir reacciones positivas de la prueba epicutánea en pacientes con DA. La ausencia de una correlación significativa de la PCP y los anticuerpos IgE específicos sugiere que la célula T y la sensibilización IgE puede estar mediado por diferentes alérgenos. No había relación significativa entre la sensibilidad CR y APD, indicando así una reactividad cruzada principal.

Palabras clave: Dermatitis atópica. Pruebas epicutáneas. Cucaracha. Reactividad cruzada con ácaros del polvo de casa.

Introduction

Cockroaches originate in Africa, Asia, and South America. In Switzerland, several species of cockroach exist, with *Blattella germanica* as the most common. Cockroaches prefer a warm and humid environment; therefore, they infest kitchens, restaurants, bakeries, farms, grocery stores, and laundries. They are active in the dark and averse to light [1].

Allergy to cockroach is an emerging problem, especially in urban communities and inner-city areas [2-8]. Several studies from many parts of the world have shown that cockroaches are an important cause of respiratory allergy and that sensitized individuals who are exposed to high levels of cockroach allergen are at risk of acute asthma attacks [9-15].

Previous and recent studies have also indicated that aeroallergens such as house dust mite, pollen, or spores might trigger atopic dermatitis (AD) [2,16-24]. Some studies have shown the existence of cross-reactivity between house dust mite and cockroach [10,13-14,25-28]. We must therefore ask whether positive diagnostic test results are only an expression of cross-reactivity by simultaneous sensitization to house dust mite.

We observed that a skin prick test (SPT) using a commercial cockroach extract (Stallergènes SA, Antony, France) in patients attending our allergy clinic was positive in 397 of 12 632

tested individuals (3.1%). This figure rose to 7.9% if only atopic individuals were considered. These results are similar to those reported by Mosimann et al [1], who showed in a group of 110 subjects living in Switzerland that 6.3% had specific immunoglobulin (Ig) E antibodies to cockroach. We aimed to investigate the role of cockroach allergen in delayed-type skin reactions in patients with AD. Several studies have shown positive SPT results and increased concentrations of specific IgE to aeroallergens in patients with AD [16-17,19,29-30].

Material and Methods

Study Population

Thirty-two subjects (23 females and 9 males) with a mean age of 30.7 years (range, 10-69 years) from our outpatient allergy clinic were enrolled in the study. After completing a standardized questionnaire and undergoing a clinical examination, participants were assigned to 1 of 2 groups: Group 1 included patients with atopic eczema (n=23) (16 females and 7 males; mean age 35.8 years; range, 14-73 years) and group 2 included nonatopic volunteers (n=9), who served as controls (7 females and 2 males; mean age, 32 years; range, 23-54 years) (Tables 1 and 2). AD was diagnosed using Hanifin and Rajka's criteria [31] and the atopy score of Diepgen et al [32] (Table 1).

Table 1. Demographic Data of the 23 Participants With Atopic Dermatitis

Patient Number	Age/Sex	Associated Allergic Diseases of the Airways	Total-IgE kU _A /L	Diepgen Score	SCORAD x/103
1	32/Male	None	119	12	26
2	29/Female	RC	51	25	43
3	30/Female	None	24	12	24
4	23/Male	RC+A	1037	14	34
5	25/Female	RC	66	18	36
6	32/Female	None	3526	22	72
7	14/Male	A	52	13	30
8	28/Female	RC+A	15569	27	57
9	51/Female	RC	506	21	14
10	38/Female	RC+A	450	24	15
11	27/Female	None	29	15	31
12	46/Female	A	26	25	58
13	27/Male	None	861	20	61
14	23/Female	RC	349	16	15
15	53/Female	RC	17	17	11
16	73/Male	None	699	11	32
17	37/Male	RC+A	129	22	59
18	36/Female	RC+A	1067	19	37
19	61/Female	A	30	25	32
20	35/Female	RC+A	1054	19	45
21	24/Female	RC+A	433	18	37
22	53/Female	RC	792	24	45
23	26/Male	RC+A	399	19	36

Abbreviations: A, asthma; Ig, immunoglobulin; RC, rhinoconjunctivitis

Table 2. Demographic Data of the 9 Nonatopic Volunteers

Patient Number	Age/Sex	Total-IgE kU _A /L
1	28/Female	13
2	26/Female	9
3	31/Female	20
4	33/Female	12
5	24/Female	22
6	32/Female	20
7	37/Female	11
8	54/Male	40
9	23/Male	3

The severity of AD was defined using the SCORAD score [33]. Patients with AD were further assigned to 2 subgroups: those with pure AD and those with AD and associated allergic diseases of the airways.

All protocols were reviewed and approved by the local ethics committee. The participants provided their signed informed consent before inclusion in the study.

Questionnaire

Possible contact with cockroaches was investigated using a questionnaire containing 16 questions on origin, domestic surroundings, occupation, and vacations (Table 3).

Table 3. Questionnaire on Possible Cockroach Contact

Where are you from?
How long have you lived in Switzerland?
Which countries have you visited?
Where did you go on your most recent trip?
What is your occupation?
What is the current situation in your apartment regarding cockroach infestation?
Has your apartment been infested before?
Has your apartment always been infested?
If there was a previous infestation, who controlled it and when?
How old is your house/apartment?
Is there a restaurant or grocery store near your apartment?
Are you working or have you worked in the food industry, catering and hotel industry, or animal fattening industry?
Are you or have you been in contact with crustaceans (crayfish, lobster, shrimp) or molluscs (snails, cuttlefish)? Do you eat this kind of food often?
Are you or have you been in contact with materials that are infested by insects (rough wool, horse hair, fodder)?
Do you have a known sensitization to house dust mite?
Do you have a known sensitization to crustaceans?

SPT

All participants underwent SPT with a panel of common aeroallergens (house dust mite; grass, birch, and mugwort pollen; cat and dog dander; *Alternaria alternata* and *Cladosporium herbarum* [Allergopharma, Reinbeck, Germany]); and cockroach (*Blattella germanica*; Stallergènes SA) following the recommendations of the European Academy of Allergy and Clinical Immunology [34].

Atopy Patch Test (APT)

Cockroach and house dust mite extracts for the APT (Stallergènes SA, Antony, France) were applied for 48 hours in patch test chambers (diameter of 16 mm; Leukotest, Beiersdorf AG, Hamburg, Germany) on clinically uninvolved skin on the back. Short-acting antihistamines were discontinued for at least 7 days before testing, and oral corticosteroids or long-acting antihistamines were discontinued for at least 6 weeks before testing. Topical corticosteroids or UV therapy had not been used in the last 4 weeks at the test application sites. To obtain minimal skin irritation, APT was applied without tape-stripping or skin abrasion. Vaseline with 0.5% urea and pure Vaseline served as negative controls. Reactions were read after 48 and 72 hours. The criteria for conventional contact allergy patch testing were used to grade positive APT reactions [35].

Total and Specific Serum IgE (CAP)

Serum samples were taken from each participant and stored at -20°C until used.

Serum levels of total and cockroach-specific IgE were measured using the Immuno CAP FEIA system according to the manufacturer's instructions (Pharmacia Diagnostics, Uppsala, Sweden).

Statistical Analysis

Statistical analysis was performed using Cohen's Kappa and 95% confidence intervals (CI) to calculate the agreement between positive APT, SPT, and CAP results. The Fisher exact test was used to assess differences in SPT, APT, and CAP results for the subgroups pure AD and AD with associated allergic diseases. Finally, the binomial parameter (PI) was estimated to determine the agreement between cockroach and house dust mite sensitization.

Results

Sensitivity to Cockroach: Correlation Between SPT, APT, IgE, and Exposure

A positive SPT result to cockroach was found in 6/23 (26%) patients with AD. Ten (43%) participants had a positive APT reaction to the cockroach extract. Specific IgE antibodies to cockroach were detected in the serum of 9 (39%) patients. Mean total IgE was 1186 kU_A/L (range, 17-15 569 kU_A/L) (Table 4).

A positive result in both APT and SPT to cockroach was found in 4 (17%) patients, and a positive APT result and elevated specific IgE levels to cockroach were observed in

Table 4. Results of SPT, Total and Specific IgE, and APT to Cockroach

	Total Participants With AD	Participants With Pure AD	Participants With AD and Additional Associated Allergic Disease	Nonatopic Control Participants
SPT-positive	6/23 (26%)	1/6 (17%)	5/17 (29%)	0/9 (0%)
CAP-positive	9/23 (39%)	2/6 (33%)	7/17 (41%)	0/9 (0%)
APT-positive	10/23 (43%)	2/6 (33%)	8/17 (47%)	0/9 (0%)
Mean total IgE	1186	755	1375	17

Abbreviations: AD, atopic dermatitis; APT, atopy patch test; CAP, specific serum IgE; Ig, immunoglobulin; SPT, skin prick test.

Table 5. Sensitization to Cockroach and House Dust Mite in 23 Patients With Atopic Dermatitis

	Positive SPT	Positive CAP	Positive APT	Total
Cockroach	6/23 (26%)	9/23 (39%)	10/23 (43%)	16/23 (70%)
House dust mite	11/23 (48%)	12/23 (52%)	11/23 (48%)	16/23 (70%)
Cockroach and house dust mite	5/23 (22%)	7/23 (30%)	6/23 (26%)	12/23 (52%)

Patient	Cockroach			Exposure in the history	House Dust Mite			Symptoms
	SPT	CAP	APT		SPT	CAP	APT	
1	-	-	+	+	+	+	-	AD
2	-	-	-	-	-	-	-	AD+R
3	-	-	-	-	-	-	+	AD
4	-	-	+	-	+	+	+	AD+R
5	-	-	-	-	-	-	-	AD+R
6	-	-	-	-	+	+	+	AD
7	-	-	+	-	-	-	+	AD+R
8	-	+	-	-	+	+	-	AD+R
9	+	+	+	-	+	+	+	AD+R
10	+	-	+	-	+	+	+	AD+R
11	-	-	-	+	-	-	-	AD
12	-	-	-	+	-	-	-	AD+R
13	-	+	-	-	+	+	-	AD
14	-	+	-	-	-	-	-	AD+R
15	-	-	+	-	-	-	+	AD+R
16	+	+	-	-	+	+	+	AD
17	+	-	+	+	-	-	-	AD+R
18	+	+	+	-	+	+	-	AD+R
19	-	-	+	+	-	-	-	AD+R
20	+	+	-	-	+	+	+	AD+R
21	-	+	-	-	+	+	-	AD+R
22	-	-	-	-	-	+	+	AD+R
23	-	+	+	-	-	-	+	AD+R

Abbreviations: AD, pure atopic dermatitis; AD+R, Atopic dermatitis with associated allergic diseases of the airways; APT, atopy patch test; CAP, specific serum IgE; Ig, immunoglobulin; SPT, skin prick test.

3 (13%) patients (Tables 5 and 6). A positive SPT result and elevated specific IgE levels to cockroach were detected in 4 (17%) patients. No statistically significant correlation was found between a positive APT result (-0.1634; 95% CI, -0.56

to 0.2331) and SPT (0.2581; 95% CI, -0.1186 to 0.6347) using CAP in participants with AD.

Five participants with AD were aware of having been exposed to cockroach (Table 5). Participant 1 was a baker

Table 6. Atopic Dermatitis and Sensitization to Cockroach: Agreement Between APT and SPT With Respect to APT

	APT+	APT-	Total
SPT+	4 (17.4%)	2 (8.7%)	6 (26.1%)
SPT-	6 (26.1%)	11 (47.8)	17 (73.9%)
Total	10 (43.5%)	13 (56.5%)	23 (100%)
CAP+	3 (13.1%)	6 (26.1%)	9 (39.1%)
CAP-	7 (30.4%)	7 (30.4%)	14 (60.9%)
Total	10 (43.5%)	13 (56.5%)	23 (100%)

Abbreviations: APT, atopy patch test; CAP, specific IgE; SPT, skin prick test.

who had reported an asymptomatic exposure to cockroach during the course of his work, although the result of APT for cockroach was positive. Participant 12 reported an infestation in her apartment 15 years previously. Participants 11, 12, 17, and 19 had been exposed to cockroach while abroad, but only participant 19 had experienced a flare-up of AD to date. A positive APT result was observed in participants 1, 17 (who also experienced a positive SPT reaction), and 19. Therefore, we identified possible sensitization to cockroach as a result of exposure during travel, at home, or at work in 5 participants.

No positive skin test reactions (SPT and APT) were observed in the nonatopic control participants (Table 4), and none of them had detectable levels of serum IgE to cockroach.

Differences Between Participants With AD and AD With Associated Allergic Diseases

Respiratory symptoms affected 17/23 (74%) participants with AD, 9 (39%) of whom had asthma (Table 5). The mean value on the Diepgen atopy score was 19 (range, 11-27), and the mean SCORAD score was 37/103 (range, 11-72/103). Six (30%) patients had pure AD. In the participants with associated allergic diseases (AD+R), a positive APT result to cockroach was found in 8/17 (47%) participants. In the group with pure AD, 2/6 (33%) patients experienced a positive result. Five (29%) of the participants with associated allergic disease (1 [17%] of whom was in the pure AD group) had a positive SPT reaction. Serum-specific cockroach antibodies were observed in 7 (41%) patients in the group with associated allergic diseases of the airways and in 2 (33%) patients in the group with pure AD. The difference in frequency of the positive SPT, APT, and CAP results for cockroach between the 2 groups was not statistically significant ($P<.62$ for SPT, $P<.40$ for APT, and $P<.65$ for CAP).

Correlation Between Cockroach and House Dust Mite Sensitization in APT, SPT, and Specific IgE

Sensitization to house dust mite was detected in 11 (48%) participants by SPT and in 11 (48%) by APT. Twelve (52%) participants had specific IgE (Table 5). Positive APT and SPT results to house dust mite were found in 6 (26%) patients, a positive APT result and elevated specific IgE antibody levels to house dust mite were found in 7 (30%) patients (Table 6). All 11 (48%) participants with a positive SPT to house dust

mite also had elevated levels of specific IgE to house dust mite. Sensitization to both cockroach and house dust mite was observed in 12 (52%) patients. Six of these participants had a positive APT result, 5 had a positive SPT result, and 7 a positive specific IgE result for cockroach and house dust mite. No correlation was found between sensitization to cockroach and house dust mite in SPT, APT, and CAP. No statistically significant differences were detected ($P<.77$ for SPT, $P<.60$ for APT, $P<1.0$ for CAP).

Discussion

Previous reports have shown positive immediate SPT and specific IgE results for aeroallergens in participants with AD [16,29-30]. Some reports indicate that aeroallergens can also induce delayed hypersensitivity reactions in patch testing and aggravate eczematous skin lesions in subjects with AD [16,19]. Roul et al [22] have demonstrated that cockroach can induce eczematous lesions in atopy patch test-positive children with AD. Thus, it was suggested that both IgE-mediated and T cell-mediated immunity are important in the pathophysiology of AD.

Our data demonstrate that cockroach often induces positive ATP reactions in adults with AD. We also show that cockroach allergen can induce a positive SPT reaction and cockroach-specific IgE in patients with AD. In a prospective European multicenter trial, Darsow et al [17] demonstrated that 83% of patients with positive SPT or specific IgE results for several aeroallergens also have a positive APT result. A positive APT result with specific IgE suggests a role of allergen-specific IgE in the development of eczematous skin lesions.

In our population, agreement between a simultaneous positive SPT result or elevated specific IgE and APT to cockroach allergen was low (4/10 and 3/10 participants, respectively, with positive APT). The data suggest that the sensitivity of T cells and IgE may be mediated by different allergens and that in T cell-mediated reactions the shift to IgE-mediated sensitivity does not always happen at the same time. The higher frequency of a positive APT result than a positive SPT result has been considered to be due to IgG-mediated sensitivity or T cell-mediated immunity. A nonspecific or toxic reaction to cockroach in APT could be possible, but no positive skin test reactions (SPT and APT) were observed in the nonatopic control participants.

Only in 4 (17%) of 6 participants with a positive SPT result to cockroach were elevated specific IgE levels to cockroach found simultaneously, although all 11 (48%) participants with a positive SPT to house dust mite also had elevated IgE to house dust mite. This suggests that the cockroach allergen used in SPT and CAP was different, unlike the house dust mite allergen used.

Clark et al [36] have also shown reactions (eczematous rash) to specific aeroallergens and described a strong correlation with aeroallergens identified in the patient's environment. In the present study, the questionnaire did not reveal infestation by or contact with cockroach in the surroundings of the 23 participants with AD, except for participant 1. Despite low exposure, we often found a positive SPT or APT result to

cockroach, and this pointed to a possible primary sensitization to house dust mite and cross-reactivity to cockroach. In earlier studies, allergic tropomyosins were found in the muscle protein of invertebrates and were identified as a major allergen with potential cross-reactivity with house dust mite. Ayuso et al [25] have shown the similarity in amino acid sequences between IgE-binding epitopes in shrimp tropomyosin Pen a 1 and cockroach Per a 7 with respect to house dust mite Der p 10 and Der f 10. Azize et al [10] detected high rates of positive SPT results for house dust mite in patients sensitized to cockroach ($P < .05$).

We show that 12 of the 23 (52%) patients with AD also had positive results for SPT, APT, and/or specific IgE to house dust mite. As no significant relationship was detected between cockroach and house dust mite, primary sensitization to cockroach and sensitization to cross-reactive allergens other than house dust mite may occur.

In conclusion, our results demonstrate that cockroach allergens can induce eczematous skin test reactions in a substantial number of patients with AD. We found no significant differences in the frequency of SPT, APT, or CAP with positive results for cockroach in participants with pure AD or in those with AD and associated allergic diseases. Except for 1 participant, we found no certain long-term exposure to explain a sensitization. The clinical relevance of sensitization to cockroach remains unclear. Positive skin test results and specific IgE concentrations as an expression of cross-reactivity through simultaneous sensitization to house dust mite seems not to be the only explanation, because some of the participants who were sensitized to cockroach were not sensitized to house dust mite and had no history of cockroach contact.

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