

## Atopic Dermatitis: Associated Factors and Contribution of Prick Tests for Etiological Diagnosis in a Sub-Saharan African Context

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### Abstract

**Background:** The contribution of allergy testing in identifying allergens responsible for atopic dermatitis flare-ups (AD) remains unexplored in Cameroon as in many other sub-Saharan African (SSA) countries, prompting us to fill this gap. The present study was undertaken to search for contributive factors, and to evaluate the contribution of prick tests in the diagnosis of AD in Cameroon.

**Methods:** We conducted a cross-sectional study from February to June 2015 in 5 hospitals of Yaoundé, the capital city of Cameroon. Participants were patients with AD, diagnosis based on anamnesis and clinical assessment during a consultation with a dermatologist, who (or their parents) gave consent to be included.

**Results:** A total of 35 patients were enrolled, including 23/35 (65.7%) females. The most represented age group was 0 - 10 years: 57.1%. Ten patients used scented soaps, and 14.3% probably had a foodborne allergy. Twenty-four patients had a family history of AD. Cotton was the type of clothing worn in 31.4% of cases. Sixteen patients had stuffed toys. Carpets were present in 19 patients' homes; dogs and cats were present in 45.7% of homes. The prick tests were performed in 29 patients, negative in 31.4% of cases. The allergens identified were: dust mites (31.0%), animal dander (24.1%), mold (24.1%) and grasses (17.2%).

**Conclusion:** The performance of prick tests identified allergens responsible for AD flare-ups in almost 2/3 of cases. Its implementation would be a considerable contribution to the proper etiological diagnosis and consequential efficient management of patients with AD in our context.

**Keywords:** Atopic Dermatitis; Allergens; Prick Test; Cameroon

### Abbreviations

AD: Atopic Dermatitis; SSA: Sub-Saharan Africa

## **Background**

Atopic dermatitis (AD), or constitutional eczema is an erythematous vesicular dermatitis occurring in an individual with atopy; it is characterized by a chronic, recurrent and sometimes disabling pruritus [1]. It represents the dermatologic manifestation of the “atopic disease” which includes also asthma, allergic rhinitis and allergic conjunctivitis [2].

AD is a type IV hypersensitivity reaction involving three actors: the allergen, antigen presenting cells and T lymphocytes [3]. It affects about one third of the general population, with greater occurrence in young children [4]. In fact, it is the most common skin disease in infants and children, affecting up to 20% of the pediatric population in some countries [5]. AD also affects adults, and can affect up to 10% of this population [5].

Despite its high frequency, AD remains a poorly known and misunderstood illness [2]. It is a benign disease but somehow troubling because it recurs in flares, under the influence of many factors. It results from the interaction between genetic and environmental factors [1]. Children with a first-degree family history of AD are more at risk of developing the condition [4]. On the other hand, contact with irritants such as scented soaps, detergents, scratchy fabrics, food allergens and airborne allergens, bacterial colonization of the skin, climatic factors, and psychological factors are able to promote AD flares [6].

The diagnosis of AD is essentially based on anamnesis and clinical assessment; no further examination is therefore essential to give the diagnosis [7]. However, patients with severe forms of AD or forms resistant to conventional therapy may require further explorations [7]. Hence the importance of allergy testing such as skin prick tests that explore the mechanisms of immediate hypersensitivity mediated by IgE immunoglobulins [8]. These tests enable identification of the precise allergens involved in order to avoid them as much as possible, with the ultimate goal of reducing AD flare-ups.

In Cameroon, data on AD are absent, and utility of skin prick tests in research of allergens remains unexplored. Willing to fill this critical gap, we carried-out the present study which purposed to explore the different factors (genetic, dietary and environmental) that may contribute to trigger or worsen AD flare-ups, and to evaluate the contribution of skin prick tests in identifying allergens responsible for AD flares in patients with AD in Cameroon, a sub-Saharan African country.

## **Methods**

### **Design and study sites**

We conducted a cross-sectional study from February to June 2015 in five hospitals of the city of Yaoundé, the political capital of Cameroon, namely: the Yaoundé Central Hospital, the Yaoundé Military Hospital, the Yaoundé University Teaching Hospital, the Biyem-Assi District Hospital, and the Elig-Essono Sub-Divisional Hospital. These centers were selected because of the presence of a dermatologist in each of them.

### **Participants**

We included all persons seen at the dermatology consultation in the different study sites, who had been diagnosed with AD by the dermatologist, and who agreed (themselves or their parents/guardians) to take part in the study. In case of diagnostic uncertainty, the patient was referred to a second study site to get the opinion of a second dermatologist, and all the discordant cases were excluded from this study. Similarly, we did not include: patients who have been taking an antihistamine drug for at least a week, those on corticosteroids (oral or injectable) for at least a month or on beta blockers for at least 48 hours before doing the prick tests; patients with extensive lesions (precluding to perform skin tests); those with an ongoing flare-up (at the time of performance of the prick test), and pregnant women. Participants were consecutively enrolled during the study period.

### Clinical diagnosis

The diagnosis of AD was based on both anamnesis and clinical evidences. The history sought existence of frequent pruritus, located with the presence of personal or family history of AD or other manifestations of the atopic disease (asthma, allergic rhinitis, or allergic conjunctivitis). The clinical diagnosis in turn reflected the topography (depending on the age of the patient) and the type of lesions: vesicles on erythematous skin progressing to oozing and formation of crusts, excoriation or lichenified plaques.

### Data collection

Once the diagnosis of AD was made, all aspects of the study were presented to patients and/or carers/guardians, and we included only those who had agreed to take part in this study. Using a structured and pre-tested standardized questionnaire, we proceeded with the collection of data. The questionnaire consisted of four parts: patient demographics (age, gender, place of residence, profession ...), its therapeutic route (prior medical or paramedical consultations, visits to traditional healers and/or therapeutic abstention), the search for factors that may contribute to trigger or worsen AD flares (type of food, type of soap used, type of clothing worn, presence of pets or stuffed toys at home, inadvertent use of antiseptics), and results of skin prick tests. Once this step was completed, an appointment was made to perform the skin tests at the same study site. Patients were asked to cease antihistamines, oral corticosteroids and beta blockers for at least 7 days, 1 month and 48 hours respectively, before the test.

### Performing prick tests

At the agreed dates and times, each patient was received to undergo a free prick test which was performed by a dermatology and allergy specialist. We always ensured beforehand that patients had observed the precautions given to them in preparation for the tests, which had been clearly specified before the appointment.

In most cases, the tests were performed on the anterior surfaces of the forearms, or on the back for the younger children. Our battery was made up of eleven allergens: dust mites (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Blomia tropicalis*); German cockroach; animal dander (cat, dog); molds (*Alternaria*, *Cladosporium*, *Aspergillus*) and grasses. This product also contained a negative control solution which is the same basic solution used to prepare the allergen extracts (but does not contain allergens), and a solution for positive control (here two solutions for positive controls were used including a histamine phosphate solution and a 9% solution of codeine phosphate).

Reading of the test was done 20 minutes after application of the last drop of allergen. The drops of allergen extracts were always cleared carefully at each site before taking dimensions. The test reading (wheal and flare) was done by measuring the mean wheal diameter using a ruler marked in millimeters. A positive or negative test result was concluded by comparing the various reactions with the controls. A prick test was negative if it did not satisfy the positivity criteria: in this case, it was comparable to the negative control. A test was positive if its diameter was larger than 3mm and the negative control remained negative.

Another method of reading was semi-quantitative involving comparison of the wheal diameter with that of the positive control. The prick test was regarded as negative if it was less than half the diameter of the positive control. It was considered positive if greater than the diameter of the positive control. Between the two, it was interpreted as weakly positive. After doing the prick tests, counseling was done to patients according to their results. If positive, it was recommended that they avoid all allergens to which they were sensitive.

### Statistical Analyses

Data were entered and encoded using Microsoft Excel 2007 software and analyzed using Epi Info version 3.5.1 (Center for Disease Control, Atlanta, USA). The results are presented as medians (interquartile range IQR) for quantitative variables, and percentages for categorical variables. Qualitative variables were compared using the Chi-squared test. The results were considered statistically significant at  $p < 0.05$ .

### Ethical Considerations

Before starting the study, an ethical clearance was issued by the Ethics Committee of the Higher Institute of Medical Technology (Yaoundé) and we obtained authorizations from the directors of the various study sites. Patients/carers/guardians were informed of the different aspects of the study and signed the informed consent form to attest that their participation in this study was voluntary and unconstrained. They could at any time decide to withdraw from the study without fear of reprisal. All necessary measures were taken to limit the risks linked with the realization of prick tests. Patients' anonymity and confidentiality of collected information were preserved. This study did not harm the physical integrity of its participants and did not interfere with their follow-up. Skin prick tests were performed for free, and the results were communicated to patients and their physicians in order to improve their management.

### Results

We recruited a total of 35 patients whose ages ranged from 0 to 43 years with a median of 10 (4 - 15) years. The most represented age range was 0 - 10 years: 57.1% (Table 1). Participants were mostly females (23/35; 65.7%), giving a M/F sex ratio of 0.52 (Table 1).

Variable	Number (N = 35)	Percentage (%)
<b>Age (years)</b>		
0 - 10	20	57.1
11 - 20	8	22.9
21 - 30	4	11.4
31 - 40	1	2.9
> 40	2	5.7
<b>Sex</b>		
Male	12	34.3
Female	23	65.7
<b>Treatment before consultation</b>		
None	10	28.6
Scented Soap	10	28.6
Traditional treatment	7	20.0
Topical corticosteroids	3	8.6
Antibiotics	3	8.6
Antifungals	3	8.6
Emollients	1	2.9

**Table 1:** Demographic characteristics of the study population and therapeutic actions before consultation.

### Factors contributing to the occurrence of AD flares

Table 2 summarizes the factors that contributed to trigger or worsen AD flares. Twenty-six patients (74.3%) had been exclusively breastfed. Diet diversification (introduction of fish, egg, peanut, soy) was begun at the age of 6 months for 48.5% of patients and at more than 6 months for 33.3% of them. Five patients (14.3%) probably had a foodborne allergy. Foods were mostly fish (8.6%), soybeans (2.9%) and eggs (2.9%; Table 2).

Factors	Number	Percentage (%)
<b>Mode of feeding at birth</b>		
• Exclusive breast feeding	26	74.3
• Mixed feeding	9	25.7
• Formula feeding	0	0.0
<b>Age when diet diversification was begun (in months)</b>		
• ≤ 3	2	6.1
• 4 - 6	20	57.1
• > 6	11	33.3
<b>Foods suspected in cases of food allergies (N=10)</b>		
• Peanuts	0	0.0
• Eggs	1	2.9
• Soy	1	2.9
• Fish	3	8.6
• Others	4	11.4
<b>Other atopic manifestations</b>		
• Asthma	4	11.4
• Allergic rhinitis	6	17.1
• Allergic conjunctivitis	6	17.1
<b>Type of soap used for baths</b>		
• Scented soaps	16	45.7
• Neutral soaps	16	45.7
• Emollient soaps	3	8.6
<b>Family history of atopic dermatitis</b>		
• First generation parent	4	11.4
• Second generation parent	3	7.6
• Twin	0	0.0
• Brother	5	14.3
• Sister	6	17.1
<b>Family history of other atopic manifestations</b>		
• Asthma	18	51.4
• Allergic rhinitis	11	31.4
• Allergic conjunctivitis	2	5.7
Number of patients who are twins	1	2.9
<b>Presence of pet animals in the home</b>		
• Cat	6	17.1
• Dog	5	14.3
• Rat	2	5.7
• Others	4	11.4
Presence of stuffed toys	16	45.7
Presence of carpets	19	54.3
<b>Type of clothing worn</b>		
• Cotton	11	31.4
• Synthetic	0	0.0
• Mixed	24	68.6
<b>Type of underwear used</b>		
• Cotton	27	77.1
• Synthetic	8	22.9
• Mixed	0	0.0

**Table 2:** Factors contributing to the occurrence of an atopic dermatitis flare.

Several other factors shown in Table 2 helped to trigger or worsen AD flares. These included: existence of atopy (allergic rhinitis, allergic conjunctivitis, asthma), use of scented soaps, history of passive smoking, type of clothing usually worn (cotton or not), possession or not of stuffed toys, carpets and pets (dogs, cats).

### Results of skin prick tests

Of the 35 enrolled patients, 2 (5.7%) did not honor their appointments to undergo the skin tests; 4 participants (11.4%) had an active flare-up which precluded them from undergoing the tests. Finally, the skin tests were performed in 29 patients (82.9%), 11 of whom (37.9%) presented negative results. The following allergens were identified: dust mites (31.0%), animal dander (24.1%), mold (24.1%) and grasses (17.2%; Table 3). Patients may have had, as shown in Table 3, a hypersensitivity to one, two or even three families of allergens at once. Thus, 13.8% of patients were sensitized to dust mites only, 10.3% both to mites and molds, and 6.9% both to molds, animal dander and grasses. Several subtypes of allergens were found (see Table 3).

Allergens	Number	Percentage (%)
<b>Families of allergens</b>		
• Dust mites only	4	13.8
• Molds only	0	0.0
• Animal dander only	3	10.3
• Grasses only	3	10.3
• Dust mites + molds	3	10.3
• Dust mites + animal dander	1	3.4
• Molds + animal dander	1	3.4
• Molds + animal dander + grasses	2	6.9
<b>Sub-types of allergens found</b>		
<b>Dust mites</b>		
• <i>Dermatophagoide pteronyssinus</i>	8	27.6
• <i>Dermatophagoide farinae</i>	8	27.6
• <i>Blomia tropicalis</i>	8	27.6
<b>Molds</b>		
• <i>Alternaria alt</i>	6	20.7
• <i>Aspergillus fumigatus</i>	6	20.7
<b>Animal dander</b>		
• Dog	7	24.1
• Cat	3	10.3
Grasses	5	17.2

**Table 3:** Families and types of allergens.

After grouping the frequency of attacks into two classes:  $\leq 1$  flare/month and  $\geq 1$  flare/month, we did not find any relationship between frequency of relapses and sensitivity to dust mites ( $p = 0.459$ ), to animal dander ( $p = 0.723$ ), to grasses ( $p = 0.723$ ), or even to molds ( $p = 0.595$ ). Similarly, there was no relationship between the frequency of relapses and the positive or negative nature of the prick test result:  $p = 0.187$ .

### Discussion

In Cameroon, few studies have been conducted on AD and none have focused on the practice of allergy investigations including the performance of prick tests to identify those allergens responsible for the occurrence or worsening of AD flare-ups. Results of this preliminary study showed that performing the prick tests permitted to incriminate the specific allergens responsible for AD flare-ups in almost

two-thirds of cases (63.1%); consequently, these tests could be an important contribution to improve the care of our patients with AD, although no etiology could be found in 37.9% of cases.

The AD affected both sexes with a female predominance (65.7%); adult subjects (22.4%) were less affected than younger people. In most cases in fact, AD tends to diminish with age and a progressive desensitization can be observed over the years [1,9]. Furthermore, we observed that before the dermatology consultation, many of our patients had either received no treatment or had used drugs that have no beneficial effect on AD. This can be explained by the fact that AD remains a poorly known and misunderstood disease for the medical staff as well as the lay man [10].

Twenty-four patients (68.6%) had a family history of AD. The study equally revealed other family atopies. This highlights a genetic predisposition to AD in our setting. The occurrence of other atopic manifestations is usual during AD, such as respiratory symptoms (asthma around age 2 to 3 years, and allergic rhinitis); this is all the more frequent when there is a first-degree family history of atopy [4]. In our series, AD was associated with allergic rhinitis, allergic conjunctivitis and asthma in respectively 17.1%, 17.1% and 11.4% of cases, which reinforces the evidence of atopy in our patients.

We found that 45.7% of patients used scented soaps for their baths, 45.7% neutral soaps and 8.6% emollient soaps. The use of aggressive detergents exacerbates alteration of the epidermal barrier due to the rise in pH of the stratum corneum. A sustained increase in the pH favors the levels and activity of proteases such as chymotrypsine, responsible for the premature hydrolysis of corneodesmosomes and decreases the activity of enzymes responsible for lipid synthesis [11,12]. It is shown that circumstances such as increased sweating through exercise or heat, skin irritation by prolonged or indiscriminate use of antiseptics (scented soaps) or unsuitable local products, or the use of wool or synthetic clothing can trigger an AD flare [1]. In our series, we observed that some of our participants wore mixed clothing (60.8%), synthetic underwear (22.9%) and others had stuffed toys (54.3%), carpets in their homes (54.3%) or lived with animals (45.7%). When we know where the various allergens we tested in our service typically reside, we realize that our patients (and/or their parents/guardians) need to be informed and educated about precautions to put in place in order to avoid as much as possible daily contact with allergens that could be a source of AD flares resistant to conventional treatments.

Skin prick tests were positive in 63.1% of cases; the allergens identified were: dust mites (31.0%), animal dander (24.1%), molds (24.1%), and grasses (17.2%). The predominance of mites may be due to poor hygiene of homes and low socioeconomic level that are characteristic of our environment. Indeed, mites live in dusty houses, particularly in carpets, rugs, fans and air conditioners; therefore they should be cleaned on a daily basis to limit exposure to allergens.

Molds and animal dander were respectively the second and third types of allergens identified in our study. We can justify these results by the fact that Cameroon is in an equatorial region with areas where the climate can be mild, hot and humid. Yaoundé, the city where the study was conducted, has this type of climate. Thus, frequently observed moisture in homes will promote mold growth in this type of climates.

Studies have been conducted in other countries on skin tests in the course of AD. A study at Tikrit Teaching Hospital of Sallah Al-deen in Iraq, conducted by Bassam, *et al.* [10] found as allergens: pollen (51%), molds (29%), mites (10%), and food allergens (4%). Similarly, a study at the General Hospital of Bali in Indonesia by Wardhana, *et al.* [13] found results comparable to ours, including 12 patients (33.3%) positive to dust mites, 10 (27.8%) to animal dander, and 9 (25%) to flower pollen. We observed in our study that only 17.2% of patients were sensitized to flower pollen. This could be due to the type of urbanization, in our context, which gives little importance to green spaces, and the fact that we do not have a floral culture/floral tradition.

The small sample size is a limitation to this study. Also to be mentioned is its cross-sectional design which did not enable us to better investigate the factors contributing to the onset of AD flares. The type of sampling (consecutive) could be an obstacle to the generalization of our findings to all Cameroonian AD patients. Further studies are needed with larger sample sizes, to better investigate the contribution of skin prick tests in the management of patients with AD in our setting.

## **Conclusion**

This preliminary study enabled us to observe that many patients with AD are exposed to many factors that can provoke or aggravate AD flares. Existence of all these factors and common habits of these patients/relatives greatly support the need for the performance of skin tests including skin prick tests in our context. These tests made it possible to identify the allergens involved in almost two-thirds of cases, which would substantially improve the care of affected patients. Dermatologists should therefore increasingly think about it for a better care of their patients, especially in cases of resistance to conventional treatments. Furthermore, this study highlights the need for raising awareness and education of patients (and/or their parents/guardians) suffering from AD so that they become aware of the precautions necessary to put in place in order to prevent or space out the occurrence and severity of AD flares.

## **Declarations**

### **Ethical approval and consent to participate**

An ethical clearance was issued by the Ethics Committee of the Higher Institute of Medical Technology (Yaoundé, Cameroon) and we obtained authorizations from the directories of the various study sites. Patients/carers/guardians were informed of the different aspects of the study and signed the informed consent form to attest that their participation in this study was voluntary and unconstrained.

### **Consent for publication**

Not applicable.

### **Availability of data and material**

Data will be made available by the corresponding author upon request.

### **Competing Interests**

The authors declare that they have no conflicts of interest with regard to this article.

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## **Authors' Contributions**

EAK and CWT conceived, designed the study and collected the data. EAK and JRNN analyzed and interpreted the data. EAK, JRNN and SAT drafted the manuscript. EAK, JRNN, IS, SAT, CWT, HA, and ECNN critically reviewed and revised the manuscript. All the authors approved the final version of the manuscript.

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