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Chapter 6

Allergic characteristics of urban schoolchildren with atopic eczema in Ghana

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Abstract

Background

Atopic eczema is an increasing clinical problem in Africa.

Objective

To determine allergic characteristics and to identify possible risk factors for eczema among schoolchildren in an urbanized area in Ghana.

Patients and Methods

Schoolchildren aged 3-16 years with eczema were recruited. For each patient, one to three age and sex-matched controls were selected. All children completed a questionnaire and were skin prick tested with a panel of allergens. Blood was drawn to determine total and allergen-specific IgE. Conditional logistic regression models with the matching factors included in the model were used to calculate the odds ratios and to adjust for possible confounders.

Results

A total of 52 children with eczema (27 boys and 25 girls) and 99 controls were included. Levels of total IgE were found to be 9.1 (1.1; 78.4) times more often elevated in children with eczema. This association was mainly driven by elevated IgE levels against cockroach antigen. Children with eczema were found to have 2.0 (0.87; 4.7) times more often positive skin prick tests (SPT), but this association diminished to 1.2 (0.40; 3.6) after adjustment for total IgE levels. Frequent washing with soap was identified as a risk factor for the development of eczema among these children.

Conclusion

Schoolchildren with eczema in Ghana were characterised by elevated IgE levels especially against cockroach antigen. The association between eczema and positive SPT was much weaker suggesting immune hyporesponsiveness of the skin. After adjustment for IgE level, SPT were less suitable to distinguish children with and without eczema.

Conflict of interest

The authors state no conflict of interest.

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Introduction

Atopic dermatitis is a chronic relapsing pruritic inflammatory skin disorder.¹⁻³ Although termed atopic, up to 60 percent of children with the clinical phenotype do not have demonstrable IgE-mediated sensitivity to allergens.² Therefore, we prefer to use the term “eczema” throughout this paper instead of “atopic dermatitis.” We have used the criteria of Hanifin and Rajka^{4,5} to define our cases with “eczema”. Eczema is widespread and its prevalence is rapidly increasing in the industrialized world.^{2,6} Eczema is also a growing clinical problem in developing countries. In West Africa the prevalence of eczema was considered to be < 5%,⁷⁻¹¹ though recent studies in West Africa and other parts of Africa have shown an increase, particularly amongst infants,¹²⁻¹⁵ perhaps because of the improvement of diagnostic measures.

The rising prevalence of eczema might be related to improved sanitation and reduction in childhood infections in developed countries, which is known as the hygiene hypothesis.¹⁶⁻¹⁹ According to this hypothesis, bacterial and viral infections in early life result in the proper maturation of the immune system, thereby reducing the expression of pro-allergic T-helper-2 (Th2) responses.¹⁹⁻²¹ Parasitic infections have also been shown to induce hyporesponsiveness and to be negatively associated with clinical atopy or allergy,^{22,23} possibly due to suppression of mast cell function.²⁴

Risk factors for eczema which are related to the hygiene hypothesis are increasing gross national per-capita income,¹¹ changes in lifestyle due to a higher socio-economic status,²⁵ reduced crowding at home,²⁶ sleeping on mattresses, changes in food consumption patterns, and more frequent washing.^{6,19,27} Eradication of endoparasites, vaccinations and the treatment of other infections may also increase the risk of eczema.^{22,23} Frequent washing can affect the skin barrier function, providing a non-immunological explanation why frequent washing may increase the risk of eczema.^{19,28-30} The growing urbanization in Africa has been associated with an increased risk of eczema,³¹ supporting the fact that changes in the environment and habits may be resulting in the allergic march, as seen in highly developed countries.

The role of atopy in the pathophysiology of eczema is still under debate.^{1,32} One hypothesis states that immunological disturbance causes IgE-mediated sensitization resulting in epithelial-barrier dysfunction as a consequence of local inflammation; the second hypothesis proposes an intrinsic defect in the epithelial cells, leading to barrier dysfunction.^{19,28-30} In the latter model, the immunologic aspects are secondary to the epithelial-barrier dysfunction and could be considered as an epiphenomenon.^{19,28-30}

The purpose of this matched case-control study was to determine the allergic characteristics of urban African schoolchildren and to identify possible risk factors for eczema in these children.

Patients and Methods

Study design

Between February and December 2005, 86 schoolchildren with moderate to severe eczema were selected at the dermatological out-patient clinics of 3 hospitals in Accra, Ghana by a dermatologist (A.H.) according to the criteria as defined by Hanifin and Rajka.^{4,5} For each included child with eczema two controls matched for age and sex without any visible symptoms of eczema were selected from the same school and class.

Study Area

Both the hospitals and schools are located in the urbanized area of the Greater Accra region of Ghana, West Africa. The study area's climate is warm with the rainy season in April to June and September to November.

Informed Consent and Ethical approval

Information sheets and consent forms were given to the cases and potential controls in school to take home to their parents. Interested parents filled the consent forms and returned them to the schools. Ethical approval was granted by the Institutional Review Board of the Noguchi Memorial Institute for Medical Research. The ethical approval number was CPN015/02-03.

Questionnaires

Questionnaire-based interviews were completed by trained staff with one of the care-takers of each child in the study. The questionnaire was adapted from the International Study of Asthma and Allergies in Childhood (ISAAC)³³ and had, among others, questions on symptoms of eczema, asthma and allergic rhino conjunctivitis, and sleeping and washing habits. The most important questions regarding eczema, asthma and allergic rhino conjunctivitis are summarized in Figure 1.

Collection and work-up of samples

All cases and controls were skin prick tested on non-affected skin of the forearm with a panel of allergens (house dust mite (*Dermatophagoides pteronyssinus*, *D. farinae*), cockroach (*Blattella germanica*), cat, dog, grass and peanuts) to determine the sensitivity of the study population to specific allergens. Peripheral blood was drawn to collect sera for the determination of the levels of total IgE (enzyme-linked-immunosorbent serologic assay) and allergen-specific IgE Immuno-CAP™ (Phadia AB, Uppsala, Sweden) in the Netherlands according to the standard protocols.

Figure 1

Three most important questions for a history of symptoms of eczema:

- (1) Has your child ever had an itchy rash which was coming and going for at least six months?
- (2) Has your child had this itchy rash at any time in the past 12 months?
- (3) Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes? The child was considered to have a history of symptoms of eczema if all three questions were answered confirmative.

Two most important questions for a history of symptoms of asthma:

- (1) Has your child had wheezing or whistling in the chest in the past 12 months?"
- (2) In the past 12 months, has wheezing ever been severe enough to limit your child's speech to only one or two words at a time between breaths? The child was considered to have a history of symptoms of asthma if the first question was answered confirmative and of severe asthma if the second question was also answered confirmative.

Two most important questions for symptoms of allergic rhino conjunctivitis:

- (1) In the past 12 months, has your child had a problem with a runny or blocked nose?
- (2) In the past 12 months, has this nose problem been accompanied by itchy-watery eyes? The child was considered to have a history of symptoms of allergic rhino conjunctivitis if both questions were answered confirmative.

The presence of malaria parasites was assessed at the Noguchi Memorial Institute, Accra by examining thick and thin blood smears for each participant. Intestinal helminth infection in stool and *Schistosoma haematobium* in urine were assessed at the same centre by standard parasitological examination.

Definition of elevated IgE tests

The values of total IgE were considered elevated when the value was 100 kU/L or higher for children who were 10 years and older; 50 kU/L or higher for children between 7 and 9 years of age; and 25 kU/L or higher for children between 4 and 6 years of age. The values of IgE specific for house dust mite, cockroach, cats dogs, peanuts and grasses were considered elevated when the value was 0.35 kU/L or higher.

Definition of positive skin prick tests

A skin prick test reaction was considered positive when the average of the longest wheal diameter (D1) and its perpendicular length (D2) was ≥ 3 mm for the test allergen

and histamine, while that to the negative control was < 3mm. The results of the skin prick tests were excluded from the analyses when the average histamine response was less than 3 mm and/or the average physiological salt response was 3 or more mm.

Statistical Methods

Logistic regression models were used to calculate odds ratios with 95 percent confidence intervals for the different variables and to adjust for possible confounders as indicated in the Tables. For all statistical analyses we used SPSS for Windows version 16.0 (SPSS Inc, Chicago, IL).

Results

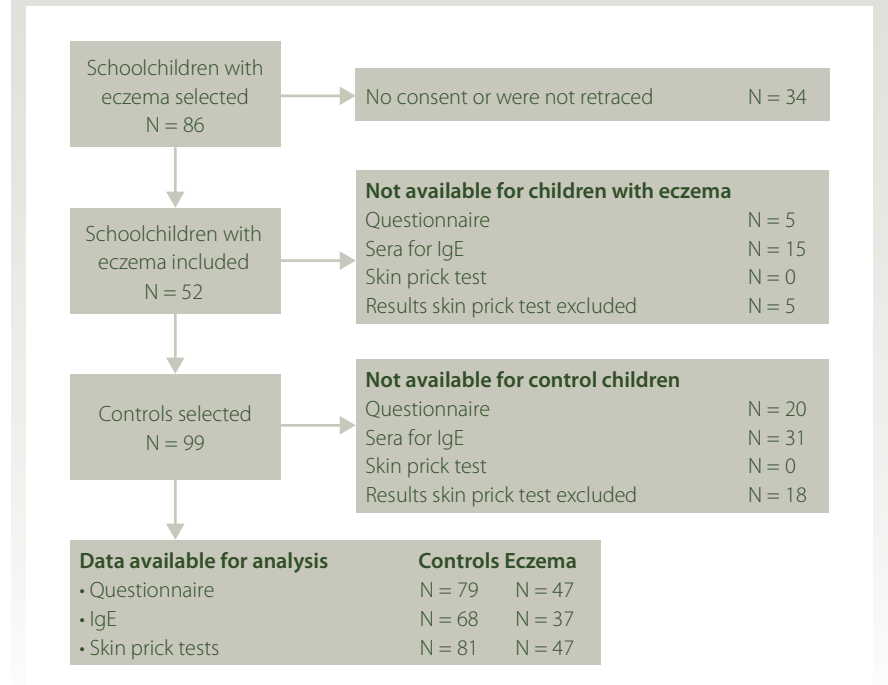
Available and missing data

A total of 52 (60.5%) out of 86 children with eczema who were initially selected for this study could be included (Figure 2). The remaining 34 children who were excluded from the study were those for whom parental consent was not obtained or could not be retraced (they had either left school, changed addresses, or simply could not be found). Accra is a typical big city in a developing country where some people have no fixed addresses and in some areas there is no proper street plan. It was, therefore, often difficult to find the children's residences. In addition, during this study only few of the parents/ caretakers had a mobile telephone, which made retracing the children difficult. Data on missing questionnaires and sera are provided in Figure 2. Skin prick tests were performed in all 52 children with eczema and all 99 control children. The results of five (9.6%) children with eczema and 18 (18.2%) control children were excluded because the response to histamine was less than 3 mm (20 boys and 2 girls) or the physiological salt controls were 3 or more mm in diameter (1 boy). Not all paired eczema-control sets were complete because of missing values for some children with eczema or their paired controls. The numbers of complete data sets of children with eczema and 1, 2 or 3 of their paired controls, respectively, which were used for analysis in the conditional logistic regression model, are provided in Fig. 2.

Baseline characteristics of the children with and without eczema

The baseline characteristics of the children are presented in Table 1. The cases and controls were well-matched. Unintentionally, however, boys with eczema and their controls were significantly younger than the girls with a mean age of the boys with eczema of 8.4 (SD 4.5) compared with a mean age of the girls with eczema of 11.0 (SD 4.2). The difference (with 95% CI) between the age of the boys and girls with eczema was 2.6 (1.3;4.0) years.

Figure 2 Child recruitment flow diagram.



Association of eczema with symptoms of eczema, asthma or allergic rhino conjunctivitis as collected by questionnaire

Using the data from questionnaire most cases reported symptoms of eczema during the last year ($P=0.003$; Table 2). Although the controls had no visible signs of eczema at the time of investigation still 9.6 % (seven of 73) of the children had reported symptoms of eczema during the last year by questionnaire (Table 2). Symptoms of asthma were not associated with eczema ($P=0.555$), but symptoms of allergic rhino conjunctivitis were more often reported among cases compared with controls ($P=0.051$; Table 2).

Association of total and allergen-specific IgE responses with eczema

Children with eczema had significantly more often elevated levels of total IgE than the controls ($P=0.023$; Table 3). This association was driven by the specific IgE response against cockroach antigen, as in the logistic regression model, the specific IgE responses against house dust mite, peanut and grasses decreased after adjustment for the IgE response against cockroach antigen (Table 3). Performing backward stepwise regression

Table 1 Baseline characteristics of the children with and without eczema.

	Controls (N = 99)	Cases (N = 52)
Sex		
Girls	51 (51.5)	25 (48.1)
Boys	48 (48.5)	27 (51.9)
Age: mean (SD)	10.1 (4.3)	9.7 (4.5)
Age categories (years)		
3 – 5	25 (25.3)	15 (28.8)
6 – 8	16 (16.2)	10 (19.2)
9 – 11	20 (20.2)	9 (17.3)
12 – 14	17 (17.2)	5 (9.6)
15 and older	21 (21.2)	13 (25.0)

Table 2 Association between the clinical characteristics of the children and the answers to the questionnaire.

	Controls (N = 73) n (% Pos)	Cases (N = 41) n (% Pos)	Odds ratios* (95% CI)
<i>Symptoms of eczema during the last year</i>			
No	66 (90.4)	10 (24.4)	1
Yes	7 (9.6)	31 (75.6)	112.9 (4.9 - 2617)
<i>Symptoms of asthma during the last year</i>			
No	62 (84.9)	33 (80.5)	1
Yes	12 (15.2)	8 (19.5)	1.3 (0.5 - ;3.6)
<i>Symptoms of severe asthma during the last year</i>			
No	70 (95.9)	38 (92.7)	1
Yes	3 (4.1)	3 (7.3)	1.9 (0.38 - 9.7)
<i>Symptoms of allergic rhino conjunctivitis during the last year</i>			
No	69 (94.5)	33 (80.5)	1
Yes	4 (5.5)	8 (19.5)	3.4 (1.0 - 11.4)

CI, Confidence Interval

*Odds ratios were calculated with a conditional logistic regression model with the matching factors included in the model.

Table 3 Distribution of elevated IgE levels in children with and without eczema.

	Controls (N = 57) N (% Pos)	Cases (N = 32) N (% Pos)	Odds ratios* (95% CI)	Adjusted odds ratios** (95% CI)
<i>Elevated total IgE #</i>				
No	18 (31.6)	2 (6.2)	1	
Yes	39 (68.4)	30 (93.8)	10.9 (1.4 - 85.0)	
<i>Elevated IgE House dust mite §</i>				
No	45 (78.9)	19 (59.4)	1	1
Yes	12 (21.1)	13 (40.6)	3.2 (1.1 - 9.3)	2.1 (0.53 - 8.2)
<i>Elevated IgE Cockroach §</i>				
No	44 (77.2)	17 (53.1)	1	1
Yes	13 (22.8)	15 (46.9)	3.9 (1.6;9.5)	4.2 (0.92 - 19.1)
<i>Elevated IgE Peanut §</i>				
No	49 (86.0)	26 (81.3)	1	1
Yes	8 (14.0)	6 (18.8)	1.7 (0.54 - 5.3)	1.3 (0.08 - 19.2)
<i>Elevated IgE Grass §</i>				
No	46 (80.7)	24 (75.0)	1	1
Yes	11 (19.3)	8 (25.0)	1.6 (0.56 - 4.3)	0.29 (0.02 - 4.4)

CI Confidence Interval

* Odds ratios were calculated with conditional logistic regression models with the matching factors included in the model.

** Odds ratios are adjusted for the other specific IgE outcomes.

Elevated total IgE when IgE ≥25 kU/L for 4-6 year old children; ≥50 kU/L for 7-9; ≥100 kU/L for 10 years and older.

§ Specific IgE elevated when IgE ≥ 0.35 kU/L.

only the specific IgE response against cockroach antigen remained in the model resulting in the non-adjusted odds ratio as presented in Table 3. Levels of cat- and dog-specific IgE antigens were too low for any conclusions (data not shown).

Association between total IgE responses and skin prick tests

Altogether 28 eczema-control sets (28 children with eczema and 48 controls) had complete data for both IgE and SPT. Not surprisingly, there was a strong association between total IgE responses and SPT ($P = 0.009$). Of the 57 (75%) children with an elevated total IgE level, 21 (36.8%) showed a positive SPT for any of the antigens tested (38.5% in the children with eczema and 35.5% without eczema: the difference between these 2% was not significant; $P = 0.816$), whereas only one child in the control group with a non-elevated total IgE level had a positive SPT. Conversely, of the 22 children with or without eczema who had a positive SPT for any of the antigens tested, all except one

Table 4 Distribution of positive skin prick tests in children with and without eczema.

	Controls (N = 81) N (% Pos)	Cases (N = 47) N (% Pos)	Odds ratios* (95% CI)	Adjusted odds ratios# (95% CI)
<i>Any skin prick test (SPT)</i>				
Negative	59 (76.6)	25 (61.0)	1	
Positive	18 (23.4)	16 (39.0)	2.0 (0.87 - 4.7)	
<i>SPT house dust mite</i>				
Negative	66 (85.7)	32 (78.06)	1	1
Positive	11 (14.3)	9 (22.0)	1.5 (0.50 - 4.6)	1.7 (0.52 - 5.2)
<i>SPT cockroach</i>				
Negative	65 (84.4)	36 (87.8)	1	1
Positive	12 (15.6)	5 (12.2)	0.84 (0.29 - 2.8)	0.74 (0.24 - 2.3)

CI, Confidence interval

*Odds ratios were calculated with a conditional logistic regression model with the matching factors included in the model.

Odds ratios are adjusted for the other SPT outcome.

child in the control group had an elevated total IgE level ($P = 0.009$). Analysing the specific IgE responses and SPT to house dust mite and cockroach antigens gave similar strong associations. The chances of having positive SPT in the presence of elevated IgE levels were 10.5 (1.3; 84.4; $P = 0.009$) for all tests together and were 82.5 (9.4; 723), $P < 0.001$ and 10.7 (2.5; 45.9), $P < 0.001$ for house dust mite and cockroach respectively.

Association between skin prick tests and eczema

A positive SPT for any of the antigens tested was associated with a 2.0 times increased risk of eczema, but statistical significance was not reached ($P = 0.104$; Table 4). Additional adjustment for total IgE level decreased this association to 1.7 (0.52; 5.2; $P = 0.391$). There was only a trend of an association with eczema when SPT for house dust mite were considered separately ($P = 0.457$), and there was no positive association with positive SPT for cockroach antigen ($P = 0.755$; Table 4). Positivity for SPT with cat, dog, grass and peanuts antigens was too low for any relevant conclusions (data not shown).

Helminth infections and malaria

With the exception of one child with eczema who showed an infection with *Schistosoma haematobium* no infections were detected with *Schistosoma mansoni*, *Ascaris lumbricoides*, *Trichuris*, hookworm, or *Enterobius vermicularis* in either the children with eczema or in the controls.

Malaria was tested in 52 eczema children and 98 controls. Malaria parasites were present in blood smears of 2 (3.8%) cases and 4 (4.1%) controls.

Association of environmental risk factors with eczema

Children with eczema were washing themselves before attending school 4 times more often than the controls and were 2 times more often sleeping on mattresses than their controls without eczema (Table 5). However, both associations did not reach statistical significance ($P=0.085$ and 0.195 ; Table 5).

Table 5 Bathing habits and sleeping place of the children in association with eczema.

	Controls (N = 73) N (% Pos)	Cases (N = 41) N (% Pos)	Odds ratios* (95% CI)
<i>Bath before school</i>			
No	12 (16.4)	2 (4.9)	1
Yes	61 (83.6)	39 (95.1)	6.3 (0.78-51.8)
<i>Sleeping on a mattress</i>			
No	29 (39.7)	11 (26.8)	1
Yes	44 (60.3)	30 (73.2)	2.0 (0.71-5.5)

CI, Confidence interval.

*Odds ratios were calculated with a conditional logistic regression model with the matching factors included in the model.

Discussion

Elevated total IgE levels were significantly associated with eczema (atopic dermatitis) among urban schoolchildren in Ghana, West Africa. The association was apparent despite the high proportion of elevated total IgE levels in children without eczema (70%). Although most children with eczema showed elevated total IgE levels, there were 2 who did not show an elevated level, suggesting that not all children with eczema had an atopic constitution.

In tropical countries, house dust mites (*Dermatophagoides pteronyssinus*) have been recognized as dominant species of clinical importance, and sensitization to house dust mite allergens could be as high as 80–90% among asthmatic and allergic people.^{34,35} Cockroach allergens are also associated with an increased risk of asthma and allergy in tropical countries.³⁶ Several allergens from house dust mites and cockroaches have been cloned and IgE cross-reactivity between the allergens of both species has been

described.³⁷ Elevated cockroach specific IgE levels appeared to be the driving force behind the association between elevated total IgE levels and eczema in our study. More than half of the children with elevated total IgE levels did not show any positive skin prick tests, suggesting immune hyporesponsiveness. The association between any positive skin prick tests and eczema was less pronounced than for elevated total IgE levels and this association importantly diminished after adjustment for elevated total IgE levels. There is increasing evidence for a causal relationship between helminth infection and reduced skin prick test responsiveness to allergens.³⁸ Unfortunately, the protective effect of helminth infections on the development of eczema, as described in earlier studies²⁰ could not be addressed in this study, since only very few children in this urban population had a helminth infection at the time of the study. We cannot exclude, however, that helminth infection in the past may have induced immune hyporesponsiveness in these children. Other environmental factors or genetic factors may be alternative explanations for the apparent immune hyporesponsiveness in these children.

We observed a non-significant positive association between frequent bathing and the presence of eczema in this study. Frequent washing with soap is considered to be a healthy exercise in Ghana. Washing with soap can impair the skin barrier function by increasing the pH of the skin surface. This increased pH of the skin induces increased activity of skin proteases, resulting in premature breakdown of the corneodesmosomes. This thinning of the stratum corneum facilitates penetration of irritants and allergens inducing an immune response.²⁷ Despite the advice to use less soap children often continue their habits, also due to the hot, humid climate and the subsequent sweating. Nevertheless, despite the frequent use of soap, the prevalence of eczema in Ghana is still very low (around 2%).³⁹ Factors such as the humid climate and other environmental factors are supposedly compensating for the frequent washing habits.

There was also a weak non-significant association between sleeping on a mattress and eczema. It is possible that parents were allowing children with eczema to sleep on a mattress more often than children without eczema and this may be even more explicit among boys. Use of mattresses could also be an indicator of socio-economic status because children slept on mattresses only when these were available in the home. Sleeping on mattresses could also lead to higher exposure to house dust mite or cockroach antigens, thus influencing the occurrence of eczema.

The difficulties that we encountered when we tried to collect complete data for all children decreased the power of our study. Nevertheless we were able to collect valuable information about eczema in Ghana which should stimulate other groups to design additional studies to examine eczema in African countries.

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