

Skin Test Reactivity to Aeroallergens in Jamaicans: Relationship to Asthma

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ABSTRACT

Background: Asthma causes significant morbidity and mortality in the developing world. It is thus important to identify modifiable risk factors.

Objectives: To undertake a cross-sectional study to determine the prevalence of skin test reactivity to aeroallergens in Jamaican children and adults and the relationship of the diagnosis of asthma to the pattern of skin test positivity.

Methods: One hundred and sixty subjects without the sickle cell gene (genotype AA), eighty adults and eighty children, were recruited. Skin testing to seven aeroallergens was undertaken (atopy being diagnosed if there were at least one positive reaction). Asthma status was determined by a questionnaire and/or medical records.

Results: Twenty-seven (34%) of the children and forty-one (51%) of the adults were skin test positive to at least one aeroallergen. The most common positive responses in both age groups were to *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus* and cockroach mix-(German and American). All adult asthmatics with current symptoms reacted to cockroach allergen.

Conclusions: Appropriate steps to reduce cockroaches and cockroach sensitization might positively impact on asthma morbidity in Jamaica.

Reactividad de la Prueba Cutánea Frente a Aeroalérgenos en los Jamaicanos: Relación con el Asma

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RESUMEN

Antecedentes: El asma causa morbilidad y mortalidad significativas en el mundo en desarrollo. Por lo tanto, es importante identificar los factores de riesgo modificables.

Objetivos: Llevar a cabo un estudio transversal a fin de determinar la prevalencia de la reactividad de la prueba cutánea frente a los aeroalérgenos en niños y adultos jamaicanos, y la relación del diagnóstico del asma con el patrón de positividad de la prueba cutánea.

Métodos: Se reclutaron ciento sesenta sujetos AA (sin genes falciformes), ochenta adultos y ochenta niños. Se llevaron a cabo pruebas cutáneas frente a siete aeroalérgenos (diagnosticándose atopia si se producía al menos una reacción positiva). El estatus asmático se determinó mediante encuestas y/o historias clínicas.

Resultados: Veintisiete (34%) de los niños y cuarenta y uno (51%) de los adultos, resultaron positivos en la prueba cutánea, al menos a un aeroalérgeno. Las respuestas positivas más comunes en ambos grupos de edad fueron frente a *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, y mezcla de cucarachas (alemanas y americanas). Todos los asmáticos adultos con síntomas usuales reaccionaron al alérgeno de la cucaracha.

Conclusiones: Medidas apropiadas a fin de reducir las cucarachas y la sensibilización a las cucarachas podría tener un impacto positivo en la morbilidad por asma en Jamaica.

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INTRODUCTION

Asthma is an important public health issue in Jamaica. Exercise-induced asthma has been reported to occur in 20 per cent of school age children (1). Asthma was diagnosed using a questionnaire in 21 per cent of 1057 Jamaican high school children, 92.7 per cent of the asthmatics reported at least one manifestation of atopy (2). In government hospitals in Jamaica, five per cent of clinic visits are asthma related and 25 per cent of respiratory admissions to hospital are due to asthma (3). Asthma is a significant cause of mortality in Jamaica, resulting in a death rate of approximately 5 per 100 000 (4). Thus, it is important to identify risk factors for asthma.

Atopy, the propensity to produce abnormal amounts of immunoglobulin (Ig) E in response to exposure to environmental allergens to which an individual has been sensitized, is the strongest identifiable risk factor for asthma with a 10 to 20 fold increase in risk in persons with a personal or family history of atopy compared with others with no such history (5, 6). Subsequent avoidance of "positive" aeroallergens might help to alleviate the symptoms of asthmatics (7, 8). The measurement of total IgE does not distinguish between atopic and non-atopic persons as there is considerable overlap in the values obtained in these two populations (9, 10). The two main methods of identifying the presence of sensitization in individuals are the measurement of allergen specific IgE *in vitro* and *in vivo* skin testing. Allergen specific IgE is measured *in vitro* by a radio-allergosorbent test (RAST). This is expensive, particularly when several allergens are assayed. This test is not available in Jamaica. In addition, in patients with symptoms of allergy, skin prick testing has been found to be more sensitive and specific than RAST (11).

Previous reports of skin prick reactivity in the Caribbean were few including three papers of 512 allergic patients from Jamaica published at least twenty years ago. Lawrence, reporting the results of skin prick testing with pollens, *D. farinae*, moulds and miscellaneous allergens, found that 98% of those tested had a reaction to pollens, 86% reacted to *D. farinae* and about two-thirds reacted to all four groups of allergens (12). No positive control (histamine) was used and it is unclear as to how the positive tests were defined. Cameron *et al* reported the results of skin testing to ten allergens in 86 patients with asthma or allergic rhinitis referred to an allergy clinic in Trinidad and Tobago. Using both positive and negative controls, and defining a positive result as any erythema \pm wheal, 65% of those tested were reactive to *D. pteronyssinus* and 58% to *D. farinae* (9). Neither of these two studies included testing to cockroach allergens. Two Barbadian studies which have been undertaken (13, 14) examined skin prick responses to only two allergens, house dust mite and mold, but not to other common allergens. The abstracts of data presented at regional meetings also report primarily on responses to house dust mite (15, 16). None of these studies included a non-allergic control group for comparison of skin prick test reactivity in those affected and unaffected by atopy.

The aims, therefore, of this study were to determine the prevalence of skin test reactivity to common aeroallergens in Jamaican adults and children and the relationship of the patterns of skin test positivity to the diagnosis of asthma (17). Patients were instructed to avoid drugs that repress skin reactivity and, using both positive and negative controls for comparison, skin prick testing to seven common aeroallergens which are known to be prevalent in the Caribbean was undertaken in a group of subjects which included a non-affected control group.

SUBJECTS AND METHODS

One hundred and sixty individuals who had been recruited without regard to a history of asthma or the relationship between asthma, atopy and sickle cell disease (SCD) were examined. The 160 individuals consisted of 80 AA (non-sickle haemoglobin genotype) adults aged between 19 and 26 years who were among those individuals followed as controls in the Jamaican Sickle Cell Cohort Study (JSCCS) (18) and eighty AA children aged five to ten years (19). The present study was of cross-sectional design and the sample tested was a convenience sample of those participating in the sickle cell study as controls. The adults had been recruited to the JSCCS at birth and were born in the same hospital on the same day as an SCD (homozygous sickle cell disease) infant and included 40 males and 40 females. The children were age-matched, neighbourhood (and thus socio-economically and environmentally similar) controls of SCD children in the sickle cell study (19) and included 37 males and 43 females. This study was approved by the Ethics Committee of the Faculty of Medical Sciences, University Hospital of the West Indies and written, informed consent was obtained from the adult participants and the parents of the children.

Protocol

All subjects were seen in a pulmonary laboratory where they underwent skin testing and completed a questionnaire.

Skin testing

The forearm was cleaned with alcohol and nine marks were placed at intervals of at least two centimetres. A drop of each aeroallergen was placed beside each mark and a different sterile 25 gauge needle was used to prick the centre of each drop. Histamine (6.0 mg/ml histamine base) and diluent (50% glycerine) were used as positive and negative controls respectively (HollisterStier Laboratories, Spokane, WA, USA 99220). The aeroallergens tested were two types of house dust mite [*Dermatophagoides farinae* (*D. farinae*) and *Dermatophagoides pteronyssinus* (*D. pteronyssinus*)], cockroach – German and American, mold mix (*Alternaria tenuis*, *Aspergillus fumigatus*, *Hormodendrum cladosporioides*, *Penicillium notatum*), Bermuda grass, cat hair and dog hair. Standardized commercial extracts (HollisterStier Laboratories, Spokane, WA, USA 99220) were used. Resuscitation equipment and drugs were available in case of anaphylaxis,

but were not required during the study. After 15 minutes, the forearm was inspected by two individuals (JK-M and NL) who independently measured and recorded the size of the wheals. A reaction was deemed positive if the resulting wheal was at least 3 mm by 3 mm, measuring the largest diameter and the diameter perpendicular to it. If there were any wheal with the negative control, a test wheal had to be at least three millimetres larger than the negative control in both diameters to be deemed positive, the method of defining positive tests used by the ISAAC study (20). Those with one or more positive reactions were diagnosed as atopic. Inter-observer reproducibility was high with concordance of reaction classification in all but six (1.0%) of 560 (80 subjects, seven allergens each) reactions in adults and in children. Reactions classified as positive by one observer and negative by the other (cat-2, cockroach-1, *D Pteronyssinus* 1, mold-1, dog-1) were treated as positive in the analysis, but additional analyses were performed to determine whether this designation impacted on the results of the study.

Questionnaire diagnosis of asthma

A modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire which had been validated in the Jamaican population was administered (19). Participants who responded positively to the question regarding a doctor's diagnosis of asthma were diagnosed as asthmatic. Adults had been followed in the clinic since birth, and those whose medical records indicated a history of at least three episodes of wheezing, at least one of which occurred after the age of six years, were also classified as having asthma. Those who reported wheezing in the past 12 months were diagnosed as current wheezers.

Statistics

Differences in positive skin test reactivity according to asthma status were assessed for statistical significance using exact logistic regression, and results presented as odds ratios with associated 95% confidence intervals. This method was adopted because, for some skin tests, there were small numbers of participants with a positive response (21). Important

and marginally important terms from univariate analysis ($p < 0.2$ in univariate analysis) were included in a multivariate regression, again using exact logistic regression, to determine whether significant associations between asthma and the reaction to a specific aeroallergen persisted after adjustment for other important allergens. The analysis was repeated coding the disparate skin test readings as negative to determine whether this affected the results. All analyses were conducted in Stata 8.2 (StataCorp, College Station, TX) and LogXact 2 (Cytel Software Corporation, Cambridge MA).

RESULTS

Twenty-seven (34%) children and forty-one (51%) adults were skin test positive to at least one aeroallergen. The most common positive reactions were to *D pteronyssinus* and *D farinae* (Table 1).

Eighteen (23%) children and 11 (14%) adults were diagnosed as asthmatic and 12 (15%) children and six (7%) adults had had asthma symptoms in the previous 12 months. Five children and one adult with current wheeze had not been previously diagnosed as having asthma. The diagnosis of asthma in the children was not significantly associated with atopy ($p = 0.80$) or with the response to any aeroallergen ($p > 0.10$ in all analyses). In adults, the diagnosis of asthma was significantly associated with reactivity to cockroach (OR 10.7, 95% CI 2.0, 110.1, $p = 0.003$) and mold (OR 7.7, 95% CI 1.6, 39.7, $p = 0.01$) and more weakly associated with reactivity to grass (OR 7.1, 95% CI 1.4, 37.5, $p = 0.02$), and atopy (OR 5.1, 95% CI 1.0, 52.0, $p = 0.06$) (Table 2). Using traditional logistic regression, a complete regression was not possible, although a logistic regression on the three most important univariate terms demonstrated that only cockroach remained statistically significant (OR 5.9 95% CI 1.0, 35.4, $p = 0.05$) whereas mold (OR 1.8 95% CI 0.3, 9.9, $p = 0.48$) and grass (OR 3.0 95% CI 0.6, 15.0, $p = 0.19$) were no longer statistically significant. On exact multivariate regression no terms remained statistically important. In adults, current wheezing was weakly associated with reactivity to cockroach ($p = 0.04$, Table 2). All atopic adults who had been diagnosed with asthma ($n = 9$) or wheezed in the past 12 months ($n = 5$)

Table 1: Distribution of the number of positive reactions

Aeroallergen	Children n (%)			Adults n (%)			Total n (%)
	Asthma Yes (n = 18)	Asthma No (n = 62)	Total	Asthma Yes (n = 13)	Asthma No (n = 67)	Total	
Cat	0 (0)	0 (0)	0 (0.0)	4 (31)	6 (9)	10 (12)	10 (6)
Cockroach	2 (11)	7 (11)	9 (11)	10 (77)	18 (27)	28 (35)	37 (23)
<i>D farinae</i>	6 (33)	13 (21)	19 (24)	6 (46)	27 (40)	33 (41)	52 (32)
<i>D pteronyssinus</i>	6 (33)	16 (26)	22 (28)	6 (46)	25 (37)	31 (39)	53 (33)
Dog	2 (11)	1 (2)	3 (4)	2 (15)	4 (6)	6 (8)	9 (6)
Grass	0 (0)	3 (5)	3 (4)	5 (38)	7 (10)	12 (15)	15 (9)
Mold	0 (0)	1(2)	1 (1)	7 (54)	7 (10)	14 (18)	15 (9)

Table 2: Relationship of asthma or wheezing to skin test positivity for individual aeroallergens using exact logistic regression.

Aeroallergen	Asthma			Wheezing		
	OR	95% CI	<i>p</i> value	OR	95% CI	<i>p</i> value
Children						
Atopy	1.3	0.4 to 4.5	0.80	1.5	0.3 to 6.2	0.75
<i>D farinae</i> positive	1.9	0.5 to 6.8	0.43	2.7	0.6 to 11.8	0.23
<i>D pteronyssinus</i> positive	1.4	0.4 to 5.0	0.73	2.1	0.5 to 9.0	0.39
Cockroach positive	1.0	0.1 to 5.9	1.00	1.7	0.2 to 11.1	0.81
Mold positive	3.4	0.0 to 134.5	1.00	5.7	0.0 to 221.3	1.00
Grass positive	0.9	0.0 to 8.5	0.92	2.9	0.1 to 61.3	0.78
Cat positive *	—	—	—	—	—	—
Dog positive	7.4	0.4 to 457.8	0.25	1.5	0.0 to 14.3	1.00
Adults						
Atopy	5.1	1.0 to 52.0	0.06	5.2	0.6 to 47.4	0.14
<i>D farinae</i> positive	1.2	0.3 to 5.3	1.00	0.7	0.1 to 5.2	1.00
<i>D pteronyssinus</i> positive	1.3	0.3 to 5.7	0.93	0.7	0.1 to 5.5	1.00
Cockroach positive	10.7	2.0 to 110.1	0.003	10.1	1.1 to 503.5	0.04
Mold positive	7.7	1.6 to 39.7	0.01	2.3	0.2 to 18.2	0.63
Grass positive	7.1	1.4 to 37.5	0.02	1.1	0.02 to 11.8	1.00
Cat positive	4.2	0.7 to 21.9	0.11	1.1	0.02 to 11.8	1.00
Dog positive	2.8	0.2 to 20.6	0.49	1.2	0.0 to 10.0	1.00

* No children reacted to cat hair

reacted to the cockroach allergen. Analysis repeated with disparate rating of skin test results coded as negative had essentially the same results (data not shown).

DISCUSSION

In a sample of Jamaican adults, a significant association between asthma and current wheezing and a positive reaction to cockroach has been demonstrated. The importance of cockroach allergen in asthma has been documented in populations outside Jamaica (22). It has been suggested that sensitization to cockroach in asthmatics may be associated with more severe disease (23). Inhalation of cockroach extract causes early, late-phase and dual responses in sensitized asthmatics (24). Sensitization to cockroach allergen may be more common in certain ethnic groups, particularly African-Americans (25), although this may be associated with poverty, social factors and inadequate access to medical facilities. There are data suggesting that this association of ethnicity with cockroach sensitization was independent of social factors (25, 26). Sadly, socio-economic data were not gathered during this research. The prevalence of cockroach sensitivity, however, is variable, being 43% in Malaysia (27) 41% in Hong Kong (28), 23% in California (29) and 20% in children from Ghana (30). The present study reports 89% sensitization in adult asthmatic Jamaicans and in all those with current symptoms. Only 40% of asthmatics from Puerto Rico were demonstrated to be sensitized to cockroach, but only a single extract of a single species, *Periplaneta americana* was used (31), whereas the authors used a mixed preparation contain-

ing extract from both the American and German cockroaches.

The prevalence estimate of skin test reactivity (33.8%) in the children herein reported is similar to findings from Australia (32.5%) (32), Nigeria (28.2%) (32), China (49%) (33) and Denmark (26% – 44%) (34). The prevalence estimate of skin test reactivity in the adults (51%) currently examined is within the range previously reported for positive responses to aeroallergens in 35.5% of adults in urban areas of the Gambia (35), 48% of Turkish adults (36) and 90% of 100 Japanese medical students (37).

In the adults, there was a trend toward an association between asthma and skin test positivity ($p = 0.08$), but there was no such trend in the children ($p = 0.6$). The lack of a relationship in the children may be explained by the heterogeneity of asthma in young children. This sample may have included those who have asthma following viral infections and who often become asymptomatic by eleven years of age (38).

There are several potential weaknesses to this study. Firstly, it examined a convenience sample which was recruited as controls in a larger SCD study; nevertheless, the authors were able to demonstrate in the adults significant associations between certain aeroallergens, particularly cockroach, and asthma. The use of the data available in the charts to classify individuals as being asthmatic based on at least three episodes of wheezing may be criticized for including those who wheezed only as young children. In fact, all but three of the 12 adults classified by their charts as having asthma (one having been classified as asthmatic based only on

questionnaire data) had at least one episode of wheezing after the age of six years, at which age “transient wheezers” are less likely to wheeze (38). Of those three, one subject was also classified as asthmatic based on his questionnaire responses. If the other two subjects are reclassified as asthmatic, the relationship between cockroach sensitivity remains (data not shown). Although there is the possibility of cross-reactivity between cockroach and other allergens, of note allergens from housedust mites (39), it must be noted that reactivity to house dust mite demonstrated no statistically significant association with asthma, and thus tropomyosin, which is common to the house dust mite and cockroach allergens, may not be the element in the cockroach allergen which is stimulating a reaction. This relationship would need to be considered if immunotherapy were contemplated (40). Secondly, the “control” children were recruited into a study examining the relationship between asthma and SCD. If there were a recruitment bias, one would have expected parents with asthmatic children to be more willing to allow their children to participate, causing a false elevation in the prevalence estimate of asthma. The prevalence of asthma in the “control” children, however, was similar to that reported in other Jamaican populations (2). Thus, the authors do not feel that there was a significant recruitment bias.

The possible relationship of cockroach sensitization to adult asthma is important, as cockroaches are ubiquitous in the Tropics. A preliminary report has suggested that immunotherapy against cockroach allergy may be useful, but this has not gained widespread acceptance (41). It is difficult to rid the home environment of cockroach antigen completely, but some success can be achieved by education and a long term commitment to eliminating cockroaches (42–44). The present study demonstrates a significant association between asthma and cockroach sensitization in a sample of Jamaican adults. While further studies may clarify whether this relationship is seen in a larger sample, appropriate steps to reduce cockroaches and cockroach sensitization in the interim may positively impact on asthma morbidity in the affected population.

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