

# ATOPY IN ASTHMATIC CHILDREN ATTENDING A TERTIARY HOSPITAL IN PRETORIA

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## ABSTRACT

**Rationale:** Asthma is said to be an atopic condition and the presence of atopy is regarded as a surrogate marker for determining asthma in a young child with chronic respiratory symptoms. However some local community findings have brought into question the association between allergy and asthma. The primary aim of this study was to document the prevalence and nature of allergy sensitivities in a group of asthmatic children attending a tertiary hospital in Pretoria, South Africa: (i) to compare them to a group of matched non-atopic children; and (ii) to compare them for co-morbid conditions present in the asthmatic children.

**Methods:** A random sample of 100 children attending the asthma clinic at Pretoria Academic Hospital was included after obtaining parental consent and patient assent. An age- and sex-matched control group of 50 non-atopic children was included. Standard allergen extracts (Alk Abelló) with negative and positive controls were administered to all children. Reactions were positive if the wheal was 3 mm greater than the negative control at 10 minutes (for inhalants) and the cut-points of Sporik were used to determine positive food reactions. All atopic children had asthma confirmed by airway hyper-responsiveness on spirometry.

**Results:** 45 asthmatic children had a positive skin-prick test (SPT). Sixteen per cent of control children had a positive SPT. The most common inhalant allergen was Bermuda grass (22%). Peanut allergy was documented in 9% of the patients.

**Conclusions:** Atopy (positive SPT and known disease) was demonstrated in only 45% of asthmatic children. This is less than many reported international studies and suggests that asthma must be associated with other environmental exposures in some areas of the world, including ours.

## INTRODUCTION

While this paper suggests that not all asthmatic children are atopic it also provides a review of the prevailing allergens in Pretoria, Gauteng.

Asthma is a complex disease.<sup>1</sup> This complexity is expressed in its aetiology, pathology, clinical expression and presentation, response to therapy and in a host of other ways. Both asthma and allergic conditions are important and increasingly common problems in our society.

While the genetic basis for asthma is poorly understood the interaction between genetics and environment in the disease's phenotypic expression is even more

obscure.<sup>1</sup> Much research work has been done on the epidemiology of preschool wheeze, giving us important insights into the 'wheezy march' of young children.<sup>2</sup> Despite attempts to develop asthma predictors for these children, studies have not yielded clinically accurate markers.<sup>3</sup> In certain studies done in the USA and Europe, allergy and atopy have proven to be somewhat helpful to distinguish asthma from postviral wheeze.<sup>3</sup> Unfortunately, though, even in the First World, where the number of causes of preschool wheeze is limited, expert panels disagree on the markers of asthma.<sup>4,5</sup>

Asthma is said to be an atopic condition; consequently the presence of atopy is regarded as a surrogate marker to determine asthma in a young child with chronic respiratory symptoms. However, some local community findings have called the association between allergy and asthma into question.<sup>6</sup>

Over time, it has become the norm to describe asthma as an atopic/allergic disease. The pathophysiology described is that, given a genetically susceptible background, allergen exposure produces atopic sensitisation. Over time, and possibly influenced by certain environmental factors, this atopic sensitisation leads to airway inflammation, which in turn leads to bronchial hyper-responsiveness and reversible airflow obstruction.

This atopic phenomenon is widely accepted as the prevailing asthma paradigm in children, whereas, among adults, asthma has traditionally been divided into 'extrinsic' and 'intrinsic' asthma. Extrinsic asthma has an atopic association. However this classification, even in adults, is not as neat as it appears since, for example, some occupational causes of asthma do not appear to involve atopy.

A number of authors have raised the concern 'that the proportion of asthma cases attributable to atopy may have been overestimated, and that other possible etiological mechanisms and risk factors for asthma may therefore have been neglected'.<sup>7</sup>

The allergens involved in atopic diseases in South Africa have been extensively studied.<sup>8-13</sup> They are pollens (from trees, grasses and weeds), animal allergens (dogs and cats), house-dust mite (HDM), insect parts, food allergens, and fungal spores. In two provinces of interest to this study (Gauteng and the Free State), atopy has been widely studied,<sup>8-13</sup> but specifically relates to individuals living in Johannesburg and Bloemfontein. Pretoria has not been investigated.

In the former Pretoria-Witwatersrand-Vereeniging region (Gauteng), studies found that atmospheric pollen was present perennially, while grass pollen, the most significant contributor was present throughout the year. Botha and Drury<sup>8</sup> found that there was no obvious seasonal variation in grass pollen sensitivity, but that grass pollen had the highest frequency of all allergens tested (48.1%). In the latest study on pollens in Bloemfontein, their allergen sensitivities were: Bermuda grass (55%), maize pollen (56%), and rye grass (37%).<sup>13</sup>

In 1990, two studies appeared to show that at high altitudes, house-dust mite played a less important role in atopy. Botha and Drury<sup>8</sup> found an HDM SPT positivity rate of only 9.5%. Erasmus<sup>9</sup> reported that HDMs

account for the lowest positivity rate of all tests, with about 25% patients testing positive. In their review of HDM allergy in South Africa, Potter *et al.*<sup>14</sup> observed that early studies had reported that although HDM sensitivity had been higher in more humid environments, it had increased in recent years and had been reported in homes with low HDM antigen levels.<sup>14</sup>

Nevertheless, later studies including the Sowetan study,<sup>10</sup> revealed an HDM SPT positivity rate of 45%. Subsequently, Davis *et al.*<sup>15</sup> reported detectable HDM antigen levels in 50% of Soweto homes – an urban environment at high altitude and with low humidity. HDM sensitivity had also increased to 44.2%.<sup>10</sup> In the latest Bloemfontein study, allergen sensitivity to mites was 24% (*Dermatophygoide pteronyssinus*), and 12% (*Lepidoglyphus destructor*).<sup>13</sup>

Allergy sensitivity (as noted by SPT positivity) to dog and cat was more common in the Free State and less common in Soweto children.<sup>10</sup> In the Bloemfontein study allergen sensitivities were: dog epithelia (19%) and cat epithelia (16%).<sup>13</sup> In an earlier study conducted in the Transvaal (Gauteng) the frequency of animal dander sensitivity was 13.2%.<sup>8</sup>

Beside sensitivity to wheat in Gauteng, the rates of SPT positivity for food allergens were much lower than for inhalant allergens (Johannesburg study).<sup>11</sup> Sensitivity to peanuts, eggs and fish was low.<sup>11</sup>

## OBJECTIVE

The primary aim of this study was to document the prevalence and nature of allergy sensitivities in a group of asthmatic children attending a tertiary hospital in Pretoria, South Africa and (i) to compare them to a group of matched non-atopic children and (ii) to compare them for comorbid conditions present in the asthmatic children.

## METHODOLOGY

A random sample of 100 children attending the asthma clinic at Pretoria Academic Hospital was included after obtaining parental consent and patient assent. An age- and sex-matched control group of 50 non-atopic children was included. Standard allergen extract tests (Alk Abelló) with negative and positive controls were conducted on all the children. The allergen extracts used were: Bermuda grass, grass mix, tree mix, dog hair dander, cat hair dander, standardised mite (*Dermatophygoide pteronyssinus*), *Blatana sp* (cockroach), cow's milk, hen's egg, wheat, fish mix, and peanut. Reactions were measured according to wheal size at 10 minutes. A wheal 3 mm greater than the negative control was regarded as a positive reaction for inhalants. Sporik's cut points were used for positive food reactions.<sup>16</sup>

Short histories of atopic clinical features were obtained from each patient. Each patient's condition was confirmed by the attending clinician and was based on clinic records and diagnostic testing. Skin-prick testing was then conducted by one of the authors. All the asthmatic children had their asthma confirmed by the American Thoracic Society (ATS) criteria for airway hyper-responsiveness by means of spirometry or response to a bronchodilator and steroid therapy (preschool children).

## RESULTS

One hundred children with asthma (67 black and 33 white) were enrolled. The age range was 2-239 months (mean 76.5, median 70.5). All children lived in the greater Pretoria (urban) area. Forty-five asthmatic children had a positive SPT. Of the 50 'control' (non-atopic) children,

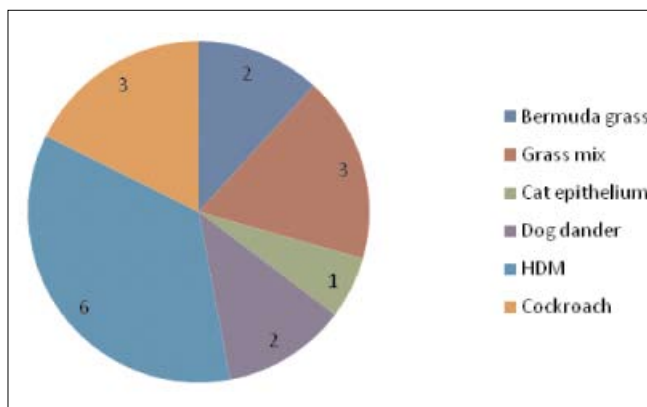


Fig. 1. SPT positivity in the control group, non-atopic children in Pretoria (N=50).

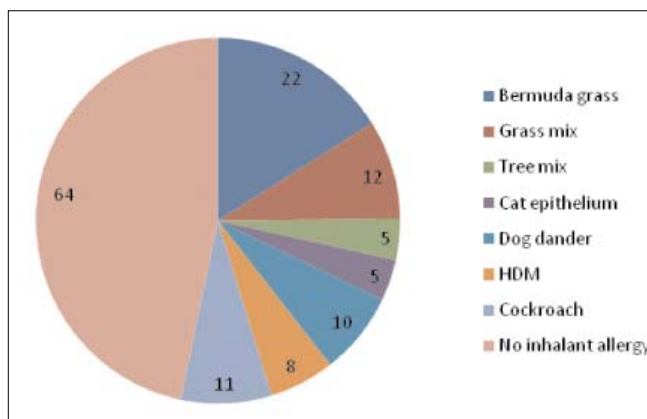


Fig. 2. SPT positivity for aero-allergens. Number of positive tests (some children having more than one positive test).

16% had a positive SPT. These allergens are reflected in Figure 1. The most common inhalant allergen in the control group of children was HDM (6 children).

### Results of inhalant allergens in the study group (Fig. 2)

The most common inhalant allergen was Bermuda grass (22%). Dog dander caused a positive SPT in 10% of patients and 5% of patients had a positive SPT to cat epithelium. Only 8% of patients demonstrated sensitivity to HDM. Cockroach allergen tested positive in 11% of children.

### Results of food allergens in the study group (Fig. 3)

The rates of SPT positivity to food allergens were much lower than those for the inhalant allergens. Peanut allergy was seen in 9% of the patients. The second most common food allergen was egg white.

## CONCLUSION

Atopy (positive SPT and known disease) was demonstrated in only 45% of asthmatic children. This is less than many reported international studies and suggests that asthma must be associated with other environmental exposures in some areas of the world, including ours. Some of these suggested aetiologies include environmental and household pollutants, dust, infective factors and diet. It is also possible that the allergens tested were incomplete and that some other allergen is important in asthma association in our region. This, however, seems unlikely.

HDM sensitivity is less common in children living in Pretoria than in those living in Johannesburg. Cockroach

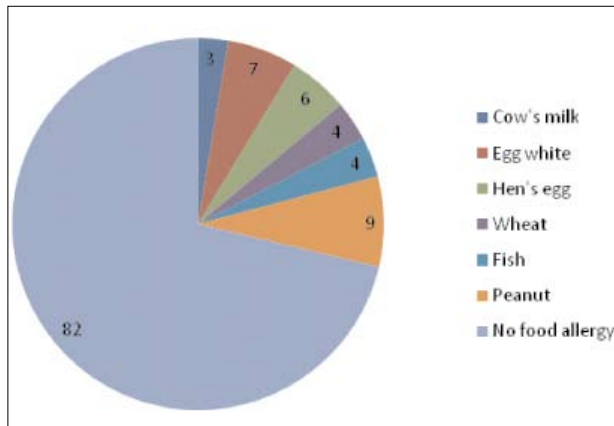


Fig. 3. SPT positivity to foods. Number of positive tests (some children having more than one positive test).

was found to be a common allergen in Pretoria which has not been fully appreciated. Children in Pretoria appear to have a greater sensitivity to dog dander than to cat epithelium. Peanut was the most common food allergen in Pretoria.

Grass sensitivity reflects the prevailing aero-allergen exposure in a typical Highveld city. However, it appears that HDM sensitivity is uncommon in Pretoria suggesting that the climate in this area is significantly adverse to mite growth. This may be the first Highveld town where microclimate does not favour mite survival. This finding can only be verified by mite studies done in Pretoria.

This study is clearly an exploratory one and has a number of significant limitations, including small sample size, inability to clearly associate sensitivity and aetiology and the lack of *in vitro* testing. Mould allergens were not included in the study as it was thought that the dry climate in this region would not support mould growth. However this study needs to be repeated using a mould testing strategy.

A further, more extensive, study of asthmatic children in our area is suggested. This study provides the motivation to explore the epidemiological associations with childhood asthma, which is important for South Africans with chest symptoms. Currently, the 'Asthma Prediction Index'<sup>3</sup> is our only tool for distinguishing postviral wheezing in young children and asthmatics. Furthermore, the scores that this index produces are largely based on allergy and atopy features. We believe that this basis may not be appropriate for our country,

nor may it be appropriate for other, similar areas of the world.

### Declaration of conflict of interest

Robin J Green is a member of the Speakers Bureau for Abbott, Aspen GSK, AstraZeneca, Boehringer Ingelheim, MSD, Nestle, Nycomed, Pfizer, Pharmaplan and Roche. He is an Advisory Board Member of Abbott, Aspen GSK, AstraZeneca, Merck, MSD, Nycomed, Pfizer, Pharmaplan and Roche. He has received funding from Abbott international, Aspen GSK and MSD. Robin Green is an executive member of ALLSA, NAEP and SATS. The other authors declare no conflict of interest.

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