

HOUSE-DUST MITES IMPACT DISEASE EXPRESSION IN CHILDREN WITH CHRONIC RHINITIS: A RETROSPECTIVE STUDY

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ABSTRACT

Background: Asthma is the most common chronic childhood disease; it affects 10–20% of South African children, with allergic rhinitis (AR) being co-morbid in up to 80%. Data are lacking on the role of allergens in low- to middle-income countries, particularly in Durban, which is located in a sub-tropical region.

Objectives: First, to determine the common allergens in children with asthma and/or AR. Secondly, to determine the prevalence of atopy and to compare disease severity in those with and without atopy.

Methods: A retrospective chart review of asthmatic and AR children over a one-year period. The GINA 2015 and ARIA guidelines were used for grading the disease severity. Laboratory tests included Phadiatop®; FX5; RAST® for individual allergens. The Fisher's exact test and the Chi-squared test were used to test for associations between disease severity and atopy. The Kruskal-Wallis rank test was used to compare allergen load and disease severity. Ethical approval was granted.

Results: One hundred children of mean age 5.5 ± 1.5 years with 60% males were enrolled. Of these, 66% were atopic, with common aeroallergens being *D pteronyssinus* (57%) and *D farina* (56%). There was an association between severity of AR and presence of *D pteronyssinus* and *D farinae* sensitisation ($p = 0.012$ and $p = 0.013$), respectively. The persistence of AR was associated with the presence of *D pteronyssinus* and *D farinae* sensitisation ($p = 0.007$ and $p = 0.009$), respectively. There was no association between severity of asthma or the persistence of asthma and the presence of aeroallergens, all with $p > 0.05$. (There was no correlation between severity or persistence of asthma based on aeroallergen sensitisation.)

Conclusion: House-dust mites (HDM) are the commonest aeroallergens and conferred more severe and persistent AR in the sub-tropical region of Durban.

INTRODUCTION

The prevalence of allergic diseases is rising worldwide, and certainly in South Africa.¹ Asthma and AR are hypersensitivity disorders of the immune system that occur through allergic inflammation induced by an allergen-specific immunoglobulin E (IgE) mediated response.² AR occurs frequently in children with a prevalence of AR of 38.5% and asthma has a prevalence of 15% among South African children.³

Asthma and AR are closely linked, and physicians are well aware of this link in the form of the 'united-airway' theory.⁴ It has been well described that co-management of these two

conditions will reduce disease severity and improve quality of life (QoL).⁴ Both these conditions form part of the united airway and management needs to be directed at both disease entities if outcomes are to improve.⁴ Aeroallergens have been implicated in the pathophysiology of both these disease processes.⁴ Those commonly implicated include HDM, grass, mould and cockroach, with a controversial minor contributor of food allergens with egg white and peanuts. Previous studies in South Africa have shown that the Oriental cockroach is the second predominant aeroallergen in KwaZulu-Natal, with sensitisation rates of 41%.⁵ The prevalence of cockroach sensitisation in atopic patients in various parts of southern Africa is similar to that

TABLE I: DEMOGRAPHIC DATA, ATOPIC STATUS AND SENSITISATION OF CHILDREN WITH ASTHMA AND AR (N = 100)

Variable	Mean	SD
Gender (M/F)*	60/40	
Ethnicity		
Indian (N)	73	
African (N)	20	
Mixed race (N)	4	
White (N)	3	
Age (months)	95	72; 206
0–23 months (N/%)	5 (5)	
24–60 months (N/%)	38 (38)	
>60 months (N/%)	57 (57)	
Height (z-scores)	–0.19	–4.53; 2.13
Weight (z-scores)	–0.08	–3.32; 5.45
BMI (z-scores)	0.07	–3.53; 6.04
Atopy (N/%)	67 (67)	
Poly-sensitisation (N/%)	63 (63)	
AR (N/%)	84 (84)	34; 175
Asthma (N/%)	78 (78)	22; 222

in Europe, the United States and Asia. In a Botswana study by Kung et al in Gaborone, cockroach sensitisation was noted in only 10% of their cohort.⁶ This is less than the prevalence of 30–70% worldwide and the reported 40% (Western Cape), 38% (KwaZulu-Natal), 32% (Free State) and 32% (Gauteng) in the provinces of South Africa.⁶

A previous study comparing patients with sensitisation to HDM found higher levels of *Blomia tropicalis* sensitisation in KwaZulu-Natal, when compared to Johannesburg.^{7,8,9} *Blomia tropicalis* sensitisation was significantly higher in northern KwaZulu-Natal, with 52% of individuals as opposed to only 2.9% for the Highveld.⁴

There are no recent data on the predominant allergens in KwaZulu-Natal; therefore we sought to describe the prevalence of allergen sensitisation in asthmatic and/or AR children in this region, with a secondary objective being to assess for the impact of allergen sensitisation on disease expression.

METHODS

SETTING

The study was a retrospective chart review conducted in a paediatric outpatient department's allergy clinic at the RK Khan Regional Hospital in Durban, KwaZulu-Natal, South Africa. KwaZulu-Natal is a sub-tropical region with a warm climate that registers temperatures ranging from 16°C to 25°C in winter and 23°C to 33°C in summer, which distinguishes it from most parts of South Africa. Durban is a coastal city at sea level with year-round humidity levels of between 71% and 83%. Children in this clinic come from both urban and peri-urban settings.

PARTICIPANTS

Participants included children who were all under the age of 14 years who were seen for follow-up between June 2014 and June 2015 with a diagnosis of asthma and/or AR. Global initiative for Asthma 2015 (GINA)¹¹ and AR and its Impact on Asthma 2014 (ARIA)¹⁷ guidelines were used for grading disease severity. Asthmatic subjects were categorised into having no asthma, mild asthma, moderate asthma and severe asthma to assess the severity of the disease as per GINA. The severity of AR was classified according to ARIA 2014 guidelines into mild intermittent disease, moderate–severe intermittent, mild persistent and moderate–severe persistent disease.

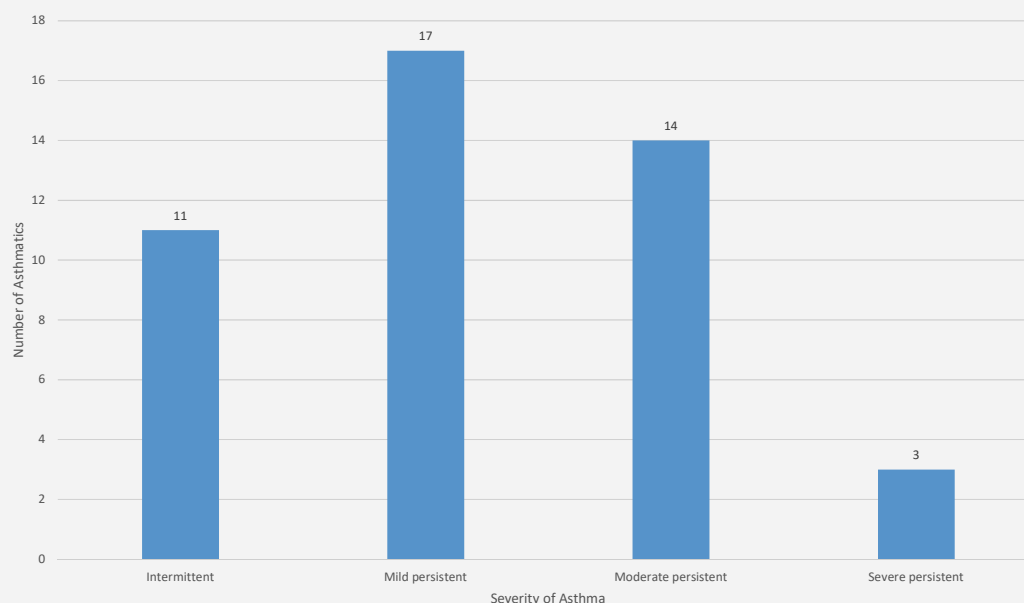


Figure 1: The severity grading for asthmatic children as per GINA (N=45)

TABLE II: CLASSIFICATION OF DISEASE SEVERITY GRADING FOR AR (N = 53)

Grading of AR	Number of subjects (%)
Mild intermittent disease	23 (43.4)
Mild persistent	26 (49.1)
Moderate–severe persistent	7 (7.5)

INVESTIGATIONS

Laboratory results were obtained from electronic system of the National Health Laboratory Service (NHLS). Tests analysed included Total IgE; Phadiatop®; FX5; RAST® for individual allergens. The universal allergy panel included both the food panel (FX5) and the inhalants panel (Phadiatop). Instruments and reagents are sourced from Thermofisher, and the method used for assessment is fluoro-enzyme immunoassay. The interpretation of results for ImmunoCap allergen mixes is qualitative values and 0.35 Ku/L is used as a cut-off. The reagents used are specific IgE conjugate (A1HFH), development solution (BW1P8), stop solution (BNDJN) and control-specific IgE (CZ4A9-1.9–3.7 Ku/L). The reagents are manufactured by Phadia AB Rapskatan, Uppsala, Sweden.

Data were analysed using the STATA statistical package (StataCorp, Version 13). Proportions were depicted as frequencies for individual aeroallergens. The Fisher's exact test and Chi-squared test were used to determine the association between aeroallergen sensitisation and disease severity. The Kruskal-Wallis equality of populations rank test was used to compare disease severity according to the different aeroallergens tested. A p-value of <0.05 was considered significant. Full ethical approval was obtained from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (IRB number: 317/15).

RESULTS

A total of 200 charts were screened, with a 100 fulfilling inclusion in the final analysis. Of the 100 excluded patients, the reasons for exclusion were: incorrect patient numbers, illegible notes, lost result sheets or duplicate blank files. There were 60% males with a mean age of 5.5 ± 1.5 years (see Table I) – 73% were children of Asian (Indian) descent. Children ranged from 0 months to 13 years, with the majority of patients in the 5–13-year age group; 5% and 38% were in the 0–2-year and 2–5-year age groups, respectively. Of the study population, the majority of subjects 73% had both asthma and AR. Only 14% had AR as a single condition and 13% asthma alone. Two-thirds (66%) were atopic, with either a food or an aeroallergen positive result. Most of the children had mild persistent asthma and mild persistent AR (see Table II and Figure 1).

Aeroallergen sensitisation was found in 60% of the study population, with the commonest aeroallergens identified being HDM: *D pteronyssinus* (56%); *D farinae* (57%), followed by cockroach mix (16%) – Figure 2. Sensitisation to food allergens was found in 26% of patients, with peanut and wheat being the most common at 17% and 10%, respectively – Figure 3. Among those identified were egg white (10%), peanuts (17%) and wheat (9%). Other aeroallergens to which patients were sensitised included dog (6%), cat (5%), Timothy grass (7%), mugwort (5%) and latex (3%).

With regard to allergens and disease severity, there was an association between the severity of AR and the presence of *D pteronyssinus* and *D farinae* ($p = 0.012$ and $p = 0.013$), respectively (see Table III). The presence of persistent AR was associated with the presence of *D*

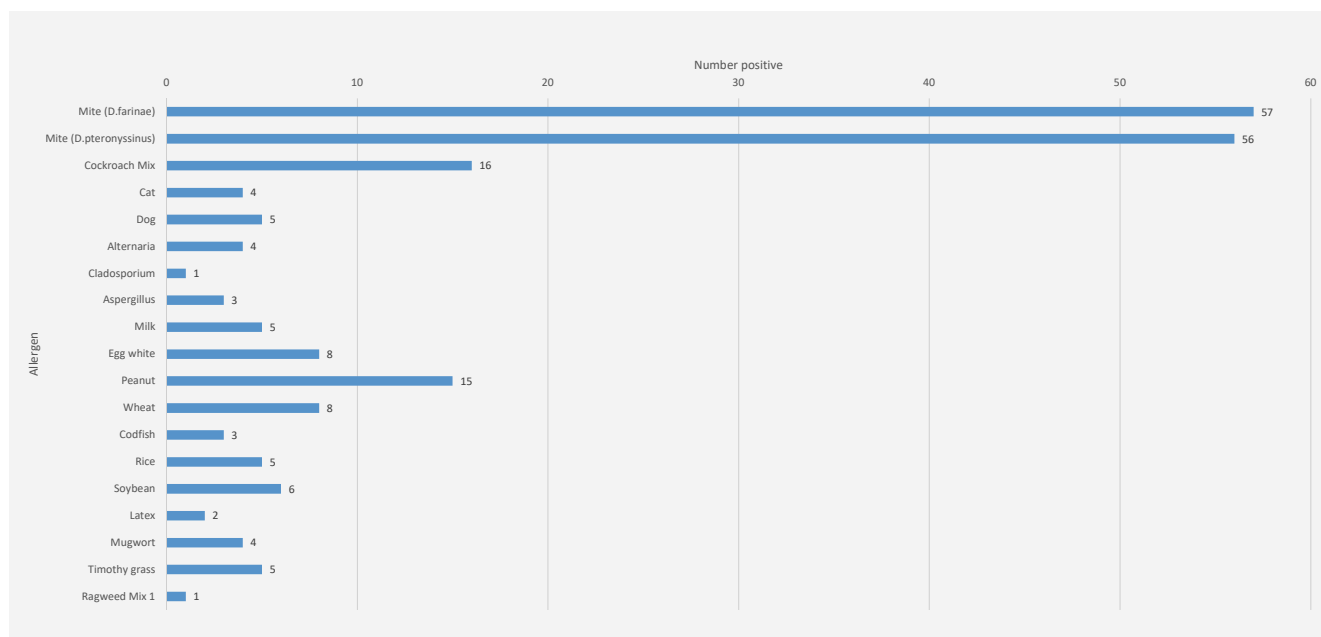


Figure 2: The predominant aeroallergens in children with asthma and allergic rhinitis. Number of children indicated at end of the column for each individual aeroallergen.

TABLE III: PRESENCE OF HDM SENSITISATION IN ASTHMA AND AR

Asthma	<i>D pteronyssinus</i> sensitisation (n)	<i>D farinae</i> sensitisation (n)
No asthma	9	10
Mild asthma	28	27
Moderate asthma	16	15
Severe asthma	4	3
AR	<i>D pteronyssinus</i> sensitisation (n)	<i>D farinae</i> sensitisation (n)
No sensitisation	2	2
Mild intermittent	38	36
Mild persistent	9	9
Moderate-severe persistent	8	8

pteronysinus and *D farina* sensitisation ($p = 0.007$ and $p = 0.009$), respectively. Persistent AR was not significantly associated with cockroach mix ($p = 0.38$). There was no association between severity and persistence of asthma with the presence of aeroallergen sensitisation: 31% of patients were monosensitised to HDM only, 38% polysensitised with other allergens out of a total of 59% sensitised to HDMs. Total IgE was not assessed owing to its limited value as a screening tool in allergy.

DISCUSSION

In the current study, we found high levels of sensitisation to common HDM in the study population, with fewer subjects sensitised to cockroach. Atopy was found in two-thirds of all children with asthma and/or AR, with three-quarters having both asthma and AR. Sensitisation to foods was present in 26% of the patients. The majority of children had mild disease, the majority of them being of Indian descent. Of significance was that the presence of HDM sensitisation was associated with more severe AR when compared to other aeroallergens, but this association was not found to be present in asthmatics.

AR and asthma frequently coexist: asthma occurs in 15–38% of patients with AR, whereas nasal symptoms are present in approximately 75% of patients with asthma.¹¹ In a Tucson study of 747 children followed up from birth to age six years, it was found that by the age of six years 42% had AR and that the onset of rhinitis in the first year of life was a risk factor for asthma by age six years.¹² A Canadian study demonstrated that 40% of AR patients have asthma, and as many as 94% of allergic asthma patients have AR.^{13,14} The current study found this association in 73% of participants. Asthma was present in 83.9% (73/87) of patients with rhinitis, whereas rhinitis was present in 84.5% (73/86) of patients with asthma.

Mites make up a large part of house-dust allergens.¹⁵ The majority of asthmatics and patients suffering from persistent AR are sensitised to mites.¹⁶ Airborne exposure

occurs with the active disturbance of contaminated fabrics and settles rapidly after disturbance.¹⁶ It has been shown that 100 mites per gram of house dust (or 2 µg of allergens per gram of dust) is sufficient to sensitise an infant.¹⁶ With approximately 500 mites per gram of house dust (or 10 µg of allergens Der p1 the major allergen of *D pteronyssinus*), the sensitised patient shows a relative risk of approximately five times for the development of asthma at a later date.¹⁶ The higher the number of mites, the earlier the first episode of wheezing.¹⁶ The prevalence of mites has been found to be higher in humid regions (20–35%) compared to relatively dry regions (15%).¹⁶ The humidity levels in Durban may explain the relatively high sensitisation of mites in this region of the country. The current study did not explore the age of onset of symptoms but the majority of children were over the age of five years.

Different mite species are found in different geographical areas. For instance, in the United States *D farinae* prevails, whereas in Western Europe the most common species is *D pteronyssinus*.¹⁷ The dominant HDM species found, *D farinae*, would be expected in a drier climate such as the Highveld of South Africa.¹⁸ HDM allergens were found in 100% of households in the Edenvale area of Gauteng, reaching levels deemed to be unsafe in 20% of households.¹⁹ Relative humidity (RH) affects HDM reproduction and survival.¹⁸ Critical equilibrium humidity (CEH) for *D pteronyssinus* is 73% at 25°C, below which dehydration occurs.¹⁸ At 40–50% RH, mites survive for only 8–11 days, which is too short for active proliferation.¹⁸ At very high RH, >85%, mites also struggle to survive because moulds proliferate in these conditions and produce toxins that may be detrimental to the mites.²⁰ Mites probably prefer a fluctuating environment, with periods of high RH to maintain water balance and low RH to minimise mould growth. In the current study, *D pteronyssinus* and *D farinae* sensitisation were found in high levels.²¹ This is in keeping with a study by Speiksma et al, which found that more humid areas of the world carry higher concentrations of these mites in households, whereas mites and their allergens are reduced in colder, more arid regions.²² HDMs are by far the most common aeroallergen implicated in allergic individuals in Asian countries:²³ the highest rates of HDM sensitisation were reported in Singapore (70 to >90%), followed by Taiwan (85–90%) and South India (89.7%).²³ The lowest sensitisation rates were described in North India (7.8%), Vietnam (9–23%) and the Philippines (33–47%).²³ Atopic Asians were mostly sensitised to the *Dermatophagoides* HDM species, with a slightly lower percentage sensitised to *Blomia tropicalis*.²⁴ However, exceptions were seen in Vietnam and Singapore in 1999, where *B tropicalis* was instead the predominant mite in sensitised atopic individuals.²³ Around the world, *B tropicalis* is abundant in the tropical and sub-tropical regions where there is high humidity and warm temperatures.⁴ A study in Mexico City, which does not have a temperate climate, showed *B tropicalis* allergy to be highly prevalent in patients with

AR and asthma.²⁴ A previous local study by Jeevarathrum et al demonstrated that allergy to *Dermatophagoides spp* occurs both on the subtropical northern KwaZulu-Natal coast of South Africa and in the temperate Highveld region, with no statistical difference between the two regions.⁴ However, the proportion of *B tropicalis* sensitisation was significantly higher in northern KwaZulu-Natal, with 52% of individuals as opposed to only 2.9% for the Highveld.⁴ The group advocated routine testing for *B tropicalis* in warm, tropical environments.⁴ Our study did not assess *B tropicalis* as it is not currently offered in the public sector as routine testing.

It has been known since at least the 1970s that atopy manifests far less in rural than in urban areas of poorer countries.^{25,26,27} Worldwide, atopy is present in up to 40% of the population.²⁸ The interactions between urbanisation, migration and the changes induced by not only direct immunological exposure to allergen, but the context of exposure, have been studied in an excellent unique study by Steinman et al.²⁹ This is the only study in the region ever to have compared allergenicity and bronchial hyperreactivity (BHR) using histamine challenges in 2 157 children, 10–14 years old, living in different areas, from the Libode district in rural Eastern Cape (former Transkei), Marconi Beam (an informal settlement area in the Western Cape) and Kirstenhof, an established city suburb in Cape Town.²⁹ There are numerous important findings from this study: 17% of rural and 34.4% of recently urbanised black children now show increased BHR (by histamine challenge) compared with 0.03% and 3.1% respectively shown 30 years ago.²⁹ This compares with the current prevalence of increased bronchial reactivity of 33% in white urban children.²⁹ The acquisition of sensitisation to one or more aeroallergens as indicated by CAP RAST tests was present in 36% of the children with normal BHR and in 62% of the children with increased BHR.²⁹ Overall atopic sensitisation to one or more aeroallergens by skin-prick test (SPT) was found in 42% of the recently urbanised Xhosa children and 45% of urbanised white children.²⁹ In a cohort of 455 asthmatic black African children at Baragwanath Hospital, Soweto, South Africa, 70% of the patients had positive SPTs to allergens,³⁰ compared with 45% in a Pretoria.³¹ The current study found the presence of atopy in 67% of the study population. Levin et al reported atopic sensitisation in 34% of urban black African children in Cape Town with asthma and AR and of these 26% were sensitised to HDM and 17% to German cockroach.³² In Cameroon, Mbatchou et al found 42% sensitisation to aeroallergens, with *D pteronyssinus* (24.2%), *D farinae* (22.8%), *B tropicalis* (23.3%) and *Blattella germanica* (15.2%) being the most common allergens found in their cross-sectional study of 600 participants.³³ With the study site being located in a coastal region at sea level, higher rates of sensitisation to HDM (42%) were demonstrated by Potter et al in a coastal study in Cape Town.^{7,34} Previous residence in a coastal region was also found in a study

in the inland province of Free State, South Africa, by Seedat et al to be a risk factor for HDM sensitisation.³⁵ A Turkish study showed that children with asthma who live at high altitudes are characterised by higher pollen but lower mite sensitisation rates than those living at sea level.³⁶ Different climatic conditions and altitudes may affect aeroallergen sensitisation in children with asthma.³⁶ The higher levels of sensitisation in our population may be explained by a combination high humidity and low altitude that favours more atopy. Whether ethnicity has an impact on sensitisation particularly to mites requires further exploration.

In West Africa (Nigeria and Ghana), a high prevalence of cockroach sensitisation was seen in asthmatic children and adolescents, and cat dander was also a more significant allergen than in Asia.²³ Atopic patients in Europe and the United States were also more highly sensitised to animal dander (cat and dog) and pollen than Asians.²³ Middle Eastern atopic subjects had the highest overall sensitisation rates to all aeroallergens – dust mites, cockroach, animal dander, pollen and mould.²³ A local Durban study conducted by Manjra et al showed that in SPTs 41% of asthmatic children in Durban were sensitised to cockroaches.³⁷ This was the second most common allergen in 16% of the current study population, but at lower levels than previously described. In a study in Germany, Lehmann et al found that *Alternaria* sensitisation was common and that it increased with age.³⁸ However, their study showed no significant correlation between asthma severity, hospitalisation rates and sensitisation profiles.³⁸ In west Sweden sensitisation to both cat and dog allergens increased the prevalence of asthma combined with rhinitis, and the number of sensitised components increased asthma severity.³⁹ We also found no correlation between these aeroallergens and disease severity.

A Korean study by Kyo Ha et al demonstrated that poly-sensitisation was weakly related to multiple morbidity.⁴⁰ However, the number of allergens to which a child is sensitised is related to the severity of IgE-mediated symptoms.⁴⁰ Most of the children in the current study were poly-sensitised but this did not correlate with disease severity. Food sensitisation was found in 26% of subjects in the current study. This is higher than the reported rates from a large epidemiological study with more than 38 000 children in the United States that showed a prevalence of 8% in children.⁴¹

The strength of the present study is that this is the first time in recent years that an attempt has been made to identify the prevalence of allergens in children in a peri-urban setting in KwaZulu-Natal. The study is, however, limited by its retrospective nature with a small sample size. Other limitations are the fact that data could not be obtained from the records for half of the patients who should have been included in the study and the limited number of allergens

for which sensitisation could be tested. The results are also reflective of black African and Indian children in a peri-urban setting in KwaZulu-Natal. There may be a bias of children with more severe disease presenting for follow-up and therefore skewing the data to reflect more severe disease in those sensitised to HDM.

RECOMMENDATIONS

We recommend that children with asthma and AR in KwaZulu-Natal should be tested for HDM sensitisation as this form of sensitisation was associated with moderate–severe persistent AR. Measures such as removing carpets for regular cleaning, and proper aeration and ventilation, may help to decrease the allergy burden and morbidity associated with AR. Adequate coverage of drains, pest control and barrier methods to decrease cockroach species are possible ways of minimising exposure.

CONCLUSION

HDM are the commonest aeroallergens and conferred more severe and persistent AR in children in KwaZulu-Natal.

This article has been peer reviewed.

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