

Sensitivity to common allergens: relation to respiratory symptoms and bronchial hyper-responsiveness in children from three different climatic areas of Australia

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Summary

In order to examine further the relation between atopy, as defined by skin-prick tests, and respiratory illness, we studied three populations of schoolchildren aged 8–11 years and living in different climatic areas of New South Wales, Australia. Skin-prick tests were performed using 13 commercial allergen extracts. Respiratory and allergic symptoms were assessed using a self-administered questionnaire to parents and bronchial hyper-responsiveness (BHR) was measured by histamine inhalation test. We defined current asthma as BHR together with symptoms of wheeze in the 12 months prior to study. Children with one or more positive skin weals of ≥ 3 mm had significantly more recent wheeze, hayfever, eczema and BHR than children with smaller weals ($P < 0.001$). In each area, 95–97% of all atopic children were sensitized to one of the following seven allergens: house dust, *Dermatophagoides farinae*, *D. pteronyssinus*, cat dander, plantain, rye grass, and *Alternaria tenuis*. Thus, these seven selected allergen extracts and a skin weal of 3 mm could be used to detect clinically relevant atopy in these populations of children. Sensitivity to house dust mite had the strongest independent association with current asthma in all three areas. The associations of other allergen sensitivities with BHR or current asthma were area dependent, indicating the influence of local allergen levels on respiratory illness in children. The potency of house dust mite sensitivity in increasing the risk of children having BHR and current asthma is confirmed.

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Introduction

Atopy, defined as skin sensitivity to common allergens, has a close association with asthma [1,2], with bronchial hyper-responsiveness (BHR) [3–5] and with other allergic disease [6] and is the major identified risk factor for these conditions. However, the relative contributions of atopic status and of local allergen levels to the presence and severity of asthmatic and allergic symptoms and BHR are not known, and the relative importance of different common allergens is not identified, although some allergens have been found to be more important [7].

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In investigating the role of allergens in asthma, population studies that incorporate a standardized measure of atopy are an essential tool. Skin-prick tests have been commonly chosen to measure atopy in populations, largely because the procedure is simple and well documented. However, the criteria by which atopy is defined are not well established and although skin-prick tests have been shown to correlate well with specific serum IgE [8–10], the relationship is influenced by many factors, including allergen concentration. To date, the minimum skin weal size used to indicate atopy remains controversial [11–13], and the number of allergens required to detect all atopic children is unknown. Because of the large number of potentially allergenic substances and wide variations in local allergen levels, the number of allergens

thought necessary in a screening panel has generally exceeded 10 and may exceed 30 [14], although recent studies in the United Kingdom and in Sweden show that mini-panels of four selected allergens detect most atopy in those countries [15,16].

In order to examine further the relation between atopy and respiratory illness, we have measured skin-prick tests to 13 common allergens, and collected information of respiratory and allergic symptoms and of BHR from three population samples of schoolchildren living in different climatic areas of New South Wales, Australia. Here we report the prevalence of atopy in each area and the relation of skin weal size to wheeze, allergic symptoms and BHR. We also report the prevalence in each area of skin reactions to the tested allergens and the importance of different allergen sensitivities in children with BHR or current asthma.

Subjects and methods

The 3581 children studied were subjects of three population studies conducted in the towns of Wagga Wagga, Belmont and Villawood, all in New South Wales, Australia. The sample studied and the methods of data collection have been described in detail [17–19].

Population

The towns selected for study were Wagga Wagga in southwestern New South Wales; Belmont, a southern suburb of Newcastle; and Villawood, a western suburb of Sydney. Wagga Wagga is in a dry inland region; Belmont is in a humid coastal region; and Villawood is in a humid hinterland with fewer sea breezes than Belmont. The mean relative humidities (9 AM–3 PM) and daily mean minimum–maximum temperatures in June are as follows: Wagga Wagga, 88–64%/4–14°C; Belmont, 78–63%/7–16°C; and Villawood, 81–54%/7–18°C [20]. The mean rain falls for June are: Wagga Wagga, 45 mm; Belmont, 116 mm; and Villawood, 77 mm.

Five separate studies were conducted: in Wagga Wagga in 1982 and 1983; in Belmont in 1982 and 1984; and in Villawood in 1986. All studies were conducted in June, except for the Wagga Wagga study in 1983, which was conducted in October. At all studies, 3rd and 4th grade schoolchildren were tested. In Villawood, 5th grade children were also included. The sampling frame comprised all primary schools within a defined geographical area and with an enrolment of 30 or more children of appropriate age. In Wagga Wagga, one-half of available schools were selected randomly; in Belmont and Villawood, all schools were selected. Informed consent was obtained from parents of all study children.

Skin-prick tests

Atopy was measured by skin-prick test reactions to 13 allergens that were commercially available in liquid form. The allergens were chosen as representative of the spectrum of common allergens to which children may be most reactive. Histamine and glycerol were used as positive and negative controls, respectively. The allergens tested (and the weight/volume indicated by the manufacturers), were house dust (ratio not supplied); the two house dust mites *Dermatophagoides farinae* (1/50) and *D. pteronyssinus* (400 AVR/ml); the animal danders of cat, dog, horse and feather mix (all 1/10); the pollens of timothy grass, rye grass, ragweed and plantain (all 1/20); and the moulds *Alternaria tenuis* and *Aspergillus fumigatus* (both 1/10). Feather mix and *D. pteronyssinus* were manufactured by Dome (Slough, U.K.) and the remainder by Hollister–Stier (Elkhart, IN). Because the *D. pteronyssinus* allergen appeared less potent than the *D. farinae* allergen, responses to these two were combined in analyses as house dust mite sensitivity.

Although batches of allergen and investigators changed occasionally between studies, the same allergen batch and the same investigator was used throughout each study. The repeatability of the skin-prick test in 267 Villawood children tested at a 3-month interval was high. The average correct classification rate (ACC) [21] and standard error for positivity for atopy was 0.94 (0.01) and for specific allergens was as follows: house dust, 0.95 (0.01); house dust mite, 0.93 (0.01); cat, 0.99 (0.01); plantain, 0.97 (0.01); rye grass, 0.95 (0.01); and *A. tenuis*, 0.97 (0.01).

Allergens were applied to the forearm, pricked and blotted using the method of Pepys [22]. After 15 min, weal size was recorded to the nearest millimetre as the long axis and its perpendicular; mean weal size was used to determine atopy. Children were regarded as being sensitized to a particular allergen if it produced a weal of ≥ 3 mm. A reaction size of 3 mm as the lower limit for positive atopy is recommended [11], and was justified in this study. Atopy was defined solely as the presence of one or more skin weal reactions of ≥ 3 mm, to any allergen, in children with a negative weal to glycerol.

Questionnaires

Each child returned a respiratory illness history questionnaire, completed by a parent. The question of wheeze was 'Has your child ever wheezed (a whistling noise that comes from the chest)?' and, if so, 'How long is it since your child last had an episode of wheeze?'. Parents were also asked 'Has your child ever had eczema? (an itchy, dry rash on face, arms or legs)' and 'Has your child ever had attacks of hay fever? (a sneezing, running or blocked nose,

sometimes with itchy eyes or nose but not associated with a cold). The question of wheeze had a high degree of repeatability (ACC 0.96) and the questions of eczema and hayfever had a moderate degree of repeatability (ACC 0.95 and 0.94, respectively) [18]. Children with wheeze in the 12 months prior to study and with BHR when tested were classified as having 'current asthma.' Children with a positive response to the question of hayfever or eczema are classified as having 'allergic symptoms.'

Bronchial responsiveness

Bronchial responsiveness was measured using the rapid inhalation method [23]. Children who had taken a beta sympathomimetic aerosol within 6 hr or theophylline compounds within 12 hr of presenting for testing were asked to withhold medication before returning for testing the next day. Lung function at baseline and following saline inhalation was recorded by Vitalograph dry spirometer, with the child standing. Forced expiratory manoeuvres were repeated until two measurements of forced expiratory volume in 1 sec (FEV₁) reproducible to 100 ml were obtained. Histamine diphosphate was administered by DeVilbiss no. 40 hand-held nebulizer using solutions of 3.1, 6.2, 25 and 50 mg/ml, in doses ranging from 0.03 to 3.9 μ mol histamine. The test was stopped if there was a fall in FEV₁ of at least 20% or if all histamine dose steps to 3.9 μ mol had been administered. Children with a fall of 10–19% after 3.9 μ mol were given a further dose to a total of 7.8 μ mol histamine. Salbutamol aerosol was administered to aid recovery when necessary.

A dose-response curve for each child was obtained by plotting the per cent change in FEV₁ from the post-saline value against the logarithm of the dose of histamine. From this curve, the dose of histamine that caused a 20% fall in FEV₁ (PD₂₀ FEV₁) was read. Only two children with an FEV₁ below 60% of expected were excluded from the test of bronchial responsiveness and these were assigned a PD₂₀ FEV₁ of 0.1 μ mol [18]. Children with a 20% fall in FEV₁ at less than 7.8 μ mol of histamine were defined as having BHR.

Statistical analysis

Data were analysed on an IBM-compatible PC using the statistical package program SAS. Ranges given for prevalence rates are those of the 95% confidence interval (CI). Chi-square analyses of contingency tables were used to determine the degree of association between categorical variables. Chi-square trend analysis was used to examine trends in proportions.

The adjusted odds ratios for risk associated with specific allergen sensitivities, defined by skin-prick test

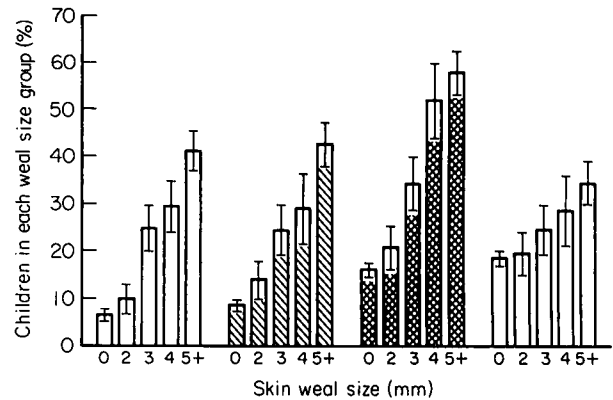


Fig. 1. Prevalence of wheeze in the previous 12 months (recent wheeze, □); bronchial hyper-responsiveness (▨); hayfever (▧) and eczema (■) in children divided into categories according to their largest skin weal recorded. The figure shows the proportion of children in each weal size group who had each symptom.

reactions of ≥ 3 mm, were calculated using logistic regression. Multiple regression analysis was used to examine collinearity between allergen sensitivities. Data for BHR, current asthma and specific allergen sensitivities were entered as categorical variable (negative or positive) in each model.

Results

In total, 3581 children were studied: 1371 in Wagga Wagga; 993 in Belmont; and 1217 in Villawood. The age of the children was 8–10 years in Wagga Wagga and Belmont, and 8–11 years in Villawood. In Villawood, 19% of the sample were aged 11 years. The numbers of boys and girls were approximately equal.

The prevalence of respiratory and allergic symptoms in children with different skin weal sizes was examined (Fig. 1). Children whose largest skin weal was ≥ 3 mm had a higher prevalence of recent wheeze, BHR and hayfever than children without positive skin weals or with small weals of 2 mm in diameter. The data thus justify the use of 3 mm as the lower limit of positive for atopy for this study and we classified children with smaller or negative skin weal reactions as non-atopic. Trend analyses showed a significant increase in the proportion of each condition with increase in skin weal size ($P < 0.001$).

Table 1 shows that the prevalence of atopy was not significantly different between areas. However, when specific allergen sensitivities were investigated, more children were sensitized to house dust mites in Belmont and Villawood, and to pollens of plantain, timothy grass, rye grass, and *A. fumigatus* in Wagga Wagga. The prevalence of sensitivity to animal danders was low, and similar in all areas.

The prevalence of BHR in children with specific

Table 1. Prevalence (%) of atopy to different allergens in children studied in three areas of Australia

Allergen	Wagga Wagga (n=1371)	Belmont (n=993)	Villawood (n=1217)
<i>D. farinae</i>	12.4* (10.7a, 14.1)	18.8 (16.4, 21.2)	19.9 (17.7, 22.1)
<i>D. pteronyssinus</i>	7.4* (6.0, 8.8)	12.7 (10.6, 14.8)	13.1 (11.2, 15.0)
House dust mite	12.8* (11.0, 14.6)	20.1 (17.6, 22.6)	21.5 (19.2, 23.8)
House dust	3.1* (2.2, 4.0)	17.6 (15.2, 20.0)	9.8 (8.1, 11.5)
Cat	2.6 (1.8, 3.4)	2.6 (1.6, 3.6)	3.6 (2.6, 4.7)
Dog	0.5 (0.1, 0.9)	0.8 (0.3, 1.4)	1.1 (0.5, 1.7)
Horse	3.0 (2.1, 3.9)	2.2 (1.3, 3.1)	1.1 (0.5, 1.7)
Feather mix	3.6 (2.6, 4.6)	8.0* (6.3, 9.7)	2.2 (1.4, 3.0)
Ragweed	4.1 (3.1, 5.2)	3.2 (2.1, 4.3)	2.2 (1.4, 3.0)
Plantain	13.9* (12.1, 15.8)	7.0 (5.4, 8.6)	5.7 (4.4, 7.0)
Timothy grass	19.1* (17.0, 21.2)	7.5 (5.9, 9.1)	11.8 (10.0, 13.6)
Rye grass	16.8* (14.8, 18.8)	6.8 (5.2, 8.4)	11.4 (9.6, 13.2)
<i>Alternaria tenuis</i>	6.2 (4.9, 7.5)	2.5 (1.5, 3.5)	4.4 (3.3, 5.6)
<i>Aspergillus fumigatus</i>	11.6* (9.9, 13.0)	4.5 (3.2, 5.8)	5.4 (4.1, 6.7)
All atopy†	30.6 (28.2, 33.0)	29.3 (26.5, 32.1)	32.8 (30.2, 35.4)

Results are the per cent with positive reactions with the 95% confidence interval in parentheses.

* $P < 0.05$ for the difference between areas indicated by the confidence intervals.

† Positive to any of the 13 tested allergens.

allergen sensitivities is shown in Table 2. Over 35% of children sensitized to house dust mite, and over 50% of children sensitized to cat dander had BHR. The prevalence of BHR in children sensitized to pollens was highest in Wagga Wagga. In each area, the prevalence of BHR was three to four times higher in atopic children than in non-atopic children.

Logistic regression was used to determine the adjusted odds ratios for children having BHR or current asthma in the presence of sensitivity to specific allergens. Initially, reactions to all 13 tested allergens were entered in a separate model for each area. We found no collinearity between specific allergen reactions. Positive reactions to dog, horse, feather mix, ragweed, timothy grass and *A. fumigatus* were not significant independent risk factors for either BHR or current asthma in any area and were then omitted. No significant interactions between specific allergen sensitivities were found in the final models. The importance of reactions to specific allergens as risk factors for BHR or current asthma are shown in Table 3. House dust mite sensitivity was a significant risk factor for both BHR and current asthma in all three areas. House dust sensitivity was a significant risk factor for BHR and current asthma in Wagga Wagga and Belmont only, and cat dander was important for BHR in Villa-

wood and for current asthma in Belmont and Villawood. Sensitivity to pollens of plantain and rye grass and to *A. tenuis* was important in Wagga Wagga only. As a result of the multiplicative effects, children living in Wagga Wagga and sensitized to house dust mite and the pollens of plantain and rye grass were 8.8 times more likely to have BHR than non-atopic children, compared with an increased risk of 2.9 in Belmont and 4.6 in Villawood.

Most atopic children were sensitized to at least one of the seven allergens which were found to have a significant association with BHR (house dust, *D. pteronyssinus*, *D. farinae*, cat dander, rye grass, plantain and *A. tenuis*). In Wagga Wagga and Belmont, 97% (CI 96%, 98%) of atopic children were sensitized to at least one of these allergens and in Villawood the proportion was 95% (CI 94%, 96%).

The distribution of skin weal size to four of the most important allergens (*D. farinae*, cat dander, rye grass and *A. tenuis*) are shown in Figs 2 and 3. In all areas, the highest prevalence and the largest skin weal reactions were to *D. farinae* and to rye grass with lower prevalence and sensitivity to cat dander and *A. tenuis*.

In atopic children, there were associations in sensitivity to certain allergens. Animal and house dust mite sensi-

Table 2. Prevalence (%) of BHR in atopic children and in children with atopy to specific allergens

Allergen	Wagga Wagga (n=1371)	Belmont (n=993)	Villawood (n=1217)
<i>D. farinae</i>	46.5* (43.9, 49.1)	40.9 (37.8, 44.0)	37.2 (34.5, 39.9)
<i>D. pteronyssinus</i>	50.5 (47.9, 53.2)	51.5 (48.4, 54.6)	39.0* (32.2, 45.8)
House dust mite	46.0 (43.4, 48.7)	39.5 (36.5, 42.5)	35.5 (28.9, 42.2)
House dust	71.4* (69.0, 73.8)	41.1 (38.0, 44.2)	34.5 (27.9, 41.1)
Cat	50.0 (47.4, 52.7)	52.0 (48.9, 55.1)	52.3 (45.4, 59.2)
Dog	28.6* (26.2, 31.0)	42.9 (39.8, 46.0)	46.2 (39.3, 53.1)
Horse	58.5* (55.9, 61.1)	38.1* (35.1, 41.1)	15.4 (10.4, 20.4)
Feather mix	44.0* (41.4, 46.6)	39.7 (36.7, 42.7)	33.3 (26.8, 39.9)
Ragweed	53.6* (51.0, 56.2)	35.5 (32.5, 38.5)	25.9 (19.8, 32.0)
Plantain	44.5* (41.9, 47.1)	31.9 (29.0, 34.8)	31.9 (25.4, 38.4)
Timothy grass	44.3* (41.7, 46.9)	28.4 (25.6, 31.2)	25.2 (19.2, 31.2)
Rye grass	50.2* (47.4, 52.7)	33.3 (30.4, 36.2)	26.6 (20.5, 32.7)
<i>Alternaria tenuis</i>	55.3* (47.6, 52.9)	44.0 (40.9, 47.1)	26.4 (20.3, 32.5)
<i>Aspergillus fumigatus</i>	50.3* (47.7, 53.0)	36.4 (33.4, 39.4)	33.3 (26.8, 39.9)
Non-atopic	10.8 (9.2, 12.4)	8.7 (7.0, 10.5)	8.2 (4.4, 12.0)
All atopy†	39.6* (37.0, 42.2)	32.8 (29.9, 35.7)	30.4 (24.0, 36.8)
Total sample	19.6 (17.5, 21.7)	15.8 (13.5, 18.1)	15.3 (10.3, 20.3)

* $P < 0.05$ for the difference between areas.

† Positive to any of the 13 tested allergens.

Table 3. Adjusted odds ratios for children with bronchial hyper-responsiveness (BHR) or current asthma (BHR plus recent symptoms) in the presence of atopy to specific allergens

Allergen	Wagga Wagga (n=1371)	Belmont (n=993)	Villawood (n=1217)
BHR			
House dust mite	1.91 (1.3, 2.9)‡	3.05 (1.9, 5.0)†	3.81 (2.6, 5.6)†
House dust	4.60 (2.1, 10.2)†	2.72 (1.7, 4.5)†	1.38 (0.8, 2.3)
Cat	0.74 (0.3, 1.7)	1.83 (0.8, 4.5)	2.53 (1.3, 5.0)‡
Plantain	1.82 (1.2, 2.7)‡	0.80 (0.4, 1.7)	1.18 (0.6, 2.3)
Rye grass	2.52 (1.7, 3.8)†	1.18 (0.6, 2.5)	1.02 (0.6, 1.8)
<i>Alternaria tenuis</i>	2.34 (1.5, 3.6)†	1.29 (0.6, 2.8)	1.62 (0.8, 3.2)
Current asthma			
House dust mite	3.54 (2.2, 5.8)†	8.05 (3.7, 17.4)†	6.42 (3.9, 10.5)†
House dust	3.75 (1.7, 8.3)†	4.19 (2.0, 8.6)†	1.10 (0.6, 2.0)
Cat	0.45 (0.2, 1.2)	3.58 (1.3, 9.6)*	4.04 (2.0, 8.2)†
Plantain	2.27 (1.4, 3.8)‡	0.38 (0.2, 1.0)*	2.25 (1.1, 4.8)*
Rye grass	2.14 (1.3, 3.6)‡	1.42 (0.5, 3.9)	0.94 (0.5, 1.8)
<i>Alternaria tenuis</i>	3.54 (2.1, 5.9)†	1.08 (0.4, 2.9)	1.23 (0.5, 2.8)

The odds ratios are given with the 95% confidence interval in parentheses.

† $P < 0.001$, ‡ $P < 0.01$, * $P < 0.05$.

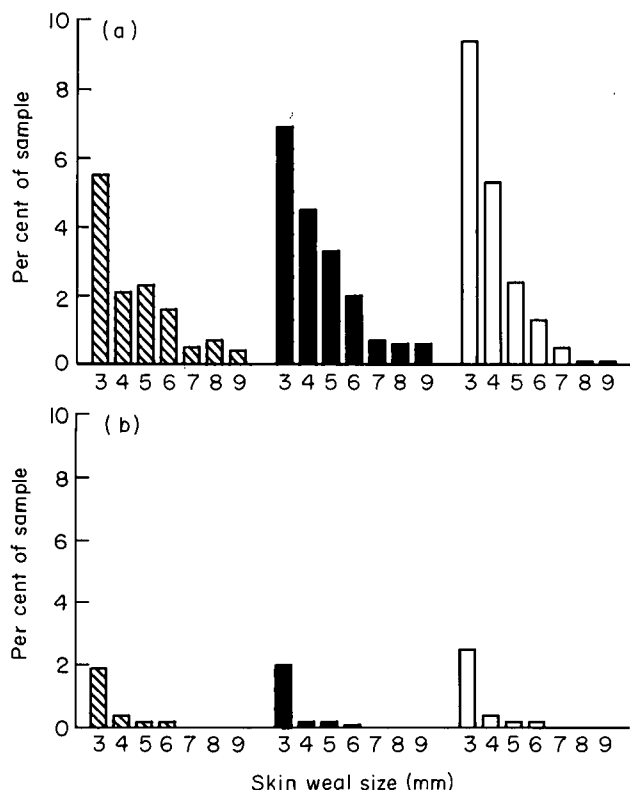


Fig. 2. Frequency distribution of size of skin weal reactions to *Dermatophagoides farinae* (a) and to cat dander (b) in Wagga Wagga (▨), Belmont (■), and Villawood (□).

vity was closely associated ($P < 0.001$); 76% of children sensitized to animals also reacted to house dust mite. Similarly, mould and pollen sensitivity was related ($P < 0.001$); 81% of children sensitized to moulds also reacted to pollens. The association in sensitivity between moulds and house dust mites, or between pollens and animals, was much weaker. Only 25% of children sensitized to animals reacted to pollens and only 22% of children sensitized to moulds reacted to house dust mite.

Discussion

Measurement of atopy by skin-prick tests has an important place in epidemiological studies of asthma. We found that a skin weal of ≥ 3 mm in diameter and a panel of seven selected allergens measured clinically relevant atopy effectively in three large populations of school-children living in different climatic areas. In each area, sensitivity to house dust mite was the most significant risk factor for children having current asthma. Sensitivity to other allergens tended to be area dependent and to have a less significant association with both BHR and current

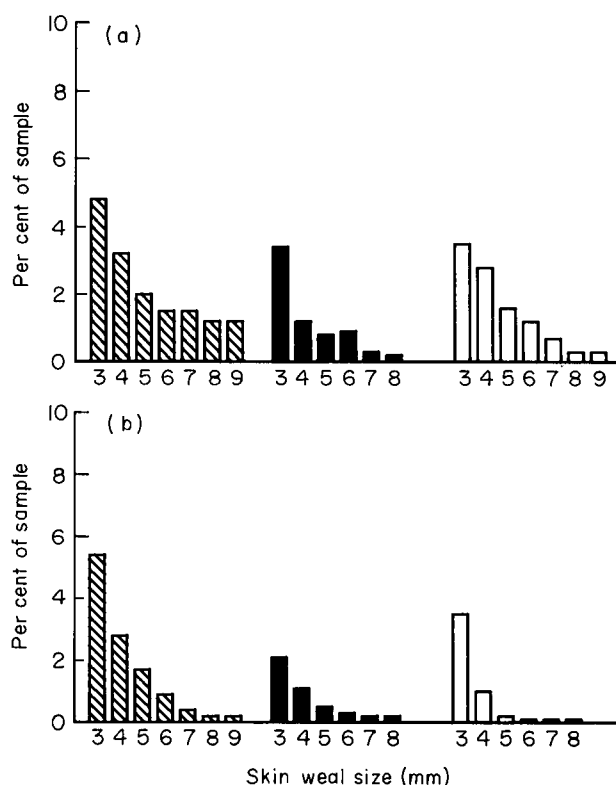


Fig. 3. Frequency distribution of size of skin weal reactions to rye grass (a) and to *Alternaria tenuis* (b) in Wagga Wagga (▨), Belmont (■), and Villawood (□).

asthma. Sensitivity to rye grass and to *A. tenuis* had a significant association with current asthma in Wagga Wagga only. Sensitivity to cat dander was associated with current asthma in Belmont and Villawood only.

Because we used methods of data collection throughout which were standardized and reliable, it is likely that reported rates of skin test reactions to allergens, of BHR and of respiratory symptoms reflect the atopic and respiratory status of children living in the three areas. The sample in each area was large and was selected randomly with a consent rate of 88% in Belmont and 83% in Wagga Wagga. Although the consent rate for study in Villawood was lower at 68%, a survey of non-attenders found no bias in terms of asthma symptoms. The 11-year-old children in Villawood were included in data analyses because their rate of atopy, respiratory symptoms and BHR was not different from the 8–10-year-old children. We recognize that the classification of children into categories of normal responsiveness and BHR is necessarily arbitrary and that BHR is neither specific nor sensitive as a test for asthma in populations [18]. However, the test of bronchial responsiveness which we used has good

repeatability under field conditions [24] and the close association between BHR and clinical asthma is well established [25]. In defining current asthma, we have chosen a definition which incorporates information of both symptoms and BHR, and which can be taken to indicate an objective measure of abnormal airway function that is associated with specific respiratory symptoms.

The size of skin weal used to define atopy is under review. In previous studies [4–6,17], we adopted definition for atopy of a skin weal of ≥ 2 mm, which was commonly used in epidemiology at that time. However, the present analyses show that small weals are clinically unimportant in that they are not associated with an increased prevalence of current wheeze, BHR or allergic symptoms. Clinical studies have also confirmed that weals > 2 mm are better used to define atopy. Because of the low precision of measuring small weals, Dreborg *et al.* [11] suggest that 3 mm should be regarded as the definition limit. Although we have reported that skin weals of 2 mm and 3 mm are not clinically important in children aged 12–14 years [5], different weal sizes may be appropriate for defining atopy at different ages because the condition appears to develop during childhood and increase in severity until early adulthood [26,27]. In this study, given the potency and composition of the allergens used, 3 mm appears to be the appropriate skin weal size to define atopy associated with allergic symptoms, current wheeze and BHR at the age of 8–11 years.

We have quantified skin-prick tests by skin weal size and by the number of reactions, which are influenced by previous allergen exposure and the number of allergens tested. Some allergens not in our panel may have increased our detection rate and may be important risk factors for respiratory illness. We did not include allergens of some commonly grown indoor and outdoor plants [28,29] or of insects such as cockroach which are known to be allergenic [30], although their association with childhood asthma is not established.

House dust was an important allergen in Wagga Wagga and Belmont, and is important in clinical studies [10,31]. However, the allergens in the extract are not known. One component may be cat allergen [32], but any soluble proteins from moulds, bacteria, animal danders, mites, algae, insects or foods could be present. It is unlikely that the Hollister–Stier house dust allergen in our panel contained house dust mite allergen, because 17% of atopic children in Belmont and 8% of atopic children in Villawood reacted to house dust allergen but not to the house dust mite allergens.

The importance of standardizing commercially available allergens is recognized [14] because many factors, including their potency, affect weal size. The *D. pteronyssinus* allergen we used was less potent than the *D. farinae*

allergen, and therefore we combined sensitivity to these two allergens in our analyses. Also, although cat dander sensitivity was an important risk factor for current asthma in two of the study areas, we found a very low prevalence of sensitivity to this allergen which has been found to be important in clinical practice [31]. It is not known why cat dander sensitivity was not important in Wagga Wagga, although its distribution was similar to the other two areas, but its low prevalence and high degree of cross-reactivity with *D. farinae* may be a factor. In other countries, animal danders are also thought important and are included in selected mini-panels [15,16].

In this study, most children sensitized to animals also reacted to house dust mites, and there was a similar linked sensitivity between moulds and pollens. Associations in sensitivities to different allergens may result from frequency of exposure, from environmental levels or from contamination of the extract. Genetic susceptibility, which could act to restrict reactivity, may also explain linked sensitivity [31]. Because it is likely that children become sensitized only to allergens encountered in their environment, cross-reactivity between house dust mite allergens is likely to have contributed to the high prevalence of sensitivity to *D. farinae*, which is uncommon in our study areas. Similarly, we found a high prevalence of sensitivity to timothy grass which is also uncommon in the study areas and which is thought to cross-react with rye grass.

There is accumulating evidence that local allergen levels influence the presence of both allergic symptoms and BHR. Epidemics of asthma which occur under unusual conditions of increased aeroallergen levels are well documented [33]. Patients who are sensitive to house dust mite are more likely to have increased symptoms when their homes have high levels of house dust mite allergen [34] and the importance of pollen levels in increasing BHR in subjects with seasonal asthma or hayfever is well documented [35,36]. Children with a predisposition to atopy presumably become sensitized when airborne allergens are encountered in sufficient levels in their environment, and it is speculated that BHR develops when the airways of sensitized subjects are repeatedly exposed to allergens. The three areas from which our study samples were drawn had different dominant aeroallergens because of their different climates. In Belmont, house dust mites numbers are high [37] and in Wagga Wagga, pollen levels have high peaks in spring [38], whereas Villawood has high levels of house dust mites and some seasonal pollens. These different characteristics were reflected in the associations between the tested allergens and BHR in each area.

Although there are many substances to which children

can become sensitized, it seems that children with an atopic predisposition are likely to develop sensitivity to a few particular allergens. We found that over 80% of atopic children were sensitized to house dust mite, rye grass or both. Because of the multiplicative effect between odds ratios for specific allergen sensitivities, children sensitized to more than one important local allergen have a greatly increased risk of having BHR or current asthma. This may explain the higher prevalence of BHR in Wagga Wagga, where house dust mite numbers are lower [37].

The importance of house dust mite sensitivity in childhood asthma is well recognized. In New Zealand, house dust mite was found to be the most important allergen associated with current asthma after adjusting for other allergens sensitivities, including pollens [7]. In a study of Australian children born to atopic parents, Van Asperen *et al.* [39] found that BHR at 7 years had a significant association with sensitivity to house dust mite and to cat, but not to pollens. It is thought that house dust mite sensitivity is important in childhood asthma because, once sensitized, children are likely to be continually exposed to high levels of small allergen particles from beds, carpets and other furnishings. Pollens may be less important because of their larger particle sizes and their intermittent presence in large quantities.

The data from these studies support the hypothesis that allergens have a perpetuating role in childhood asthma, and the potency of house dust mite allergen in this respect is confirmed. There were an equal proportion of atopic children in each area and thus local allergen levels presumably act to influence specific sensitivities, which in turn are associated with BHR and current asthma. Because sensitivity to house dust mites is potentially avoidable, it is important to determine the extent to which reduction of their allergenicity, or therapy to minimize their effects, can decrease the expression of asthma in children.

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