

Prevalence of Bronchial Hyperresponsiveness in Children: The Relationship between Asthma and Skin Reactivity to Allergens in Two Communities

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A coastal population mainly reactive to house dust mite was compared with an inland population mainly reactive to other allergens to investigate whether exposure to house dust mite plays a part in initiating childhood asthma. Respiratory symptoms, asthma, bronchial hyperresponsiveness, hay fever and atopy were all more common in the dry inland area than in the humid coastal area. In both areas 38% of children were atopic. Coastal children had more skin reactivity to house dust mites and inland children were more reactive to grass pollen extracts. The findings suggest that the clinical presentation of asthma may be related more to the total burden of aeroallergens than to exposure to a particular allergen.

The relationship between asthma and atopic status, as measured by skin reactivity to common allergens, is not fully understood. Asthma is commonly associated with allergic rhinitis in adults^{1,2} and to a lesser extent in children.^{3,4} Up to 84% of adult asthmatics have positive skin test reactions to common allergens compared with 30–40% of the general population.^{5–7} The majority of asthmatic children also have positive skin test reactivity.^{8,9} Allergens, when used in bronchial challenge studies, provoke bronchial obstruction in many asthmatic subjects.¹⁰ However, it is not known if they play a role in the production of the underlying bronchial hyperresponsiveness which is characteristic of asthma.^{11,12} The house dust mite is the allergen commonly cited as a causative factor in childhood asthma because of the high prevalence of cutaneous hypersensitivity in known asthmatics.^{8,13}

One of the aims of this study was to assess the relative effects of individual allergens, including house dust

mite, and other risk factors on the distribution of asthma. We have studied the prevalences of respiratory symptoms, bronchial hyperresponsiveness (BHR) and skin responses to a range of allergens in a humid coastal area and compared them with the prevalences found in a similar group living in a dry inland area. If exposure to house dust mite initiates BHR, then atopic populations that are mainly reactive to house dust mite allergens might be expected to have more asthma than populations mainly reactive to other allergens.

METHODS

Population Sampling

The rural towns chosen were Wagga Wagga (population 40000) and Belmont (population 20000). Wagga Wagga is an inland city 300 miles south west of Sydney with an average rainfall of 553 mm and humidity between 29 and 67%. Belmont is a southern suburb of the east coast city of Newcastle with an average rainfall of 1211 mm and humidity between 62 and 74%.

We estimated that at least 700 children would need to be studied in each area to detect a difference of 5% in the prevalence of asthma between the two populations ($\alpha = 0.05$, $\beta = 0.8$).¹⁴ The Wagga Wagga sample of 769 children was approximately half the school-

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children in years 3 and 4. In Belmont the largest 8 of 10 available schools were visited and 718 children were studied. The compliance rate was 83% of those sampled in Wagga Wagga and 88% in Belmont. Both studies were carried out in June 1982.

Data Collection

A self-administered questionnaire, together with a consent form, was completed by parents of sampled children. The reproducibility of the questionnaire had been previously established in a pilot study in Sydney (unpublished data). Details of town of birth and subsequent places of residence were requested. Questions asked whether the child had ever wheezed, had ever had attacks of wheezing during or after exercise, had ever had attacks of breathlessness, or a dry cough at night that was not associated with a cold or chest infection. The questionnaire also asked whether the child had ever been diagnosed as having asthma by a doctor or at a hospital. Parents were asked further questions about the age of onset, period since last episode and frequency of attacks for both wheezing and asthma and for details of past and current medication. Questions about bronchitis before the age of two years, hay fever and eczema were also included. Information about recent respiratory infection and recent medicine for asthma was recorded at the time of the study and height was measured without shoes.

Bronchial hyperresponsiveness to histamine was measured using the method developed for field studies by Yan *et al.*¹⁵ A group of five examiners performed the challenges in both areas. Briefly, normal resting spirometric function was measured using a Vitalograph after which saline and increasing doses of histamine were administered from a De Vilbiss nebuliser. One minute after each dose spirometric function was remeasured. Post-saline FEV1 was used to calculate percentage fall in FEV1 after increasing doses of histamine. The test was stopped when the FEV1 had fallen by 20% or after 7.8 μmol of histamine had been given. If a fall occurred a bronchodilator was given to aid recovery. A dose response curve was plotted from which the dose of histamine that caused a 20% fall in FEV1 (PD20FEV1) was extrapolated. BHR was classified as being moderate to severe if the PD20FEV1 was less than 4.0 μmol and mild if PD20FEV1 was between 4.0 and 7.8 μmol . Children with a history of wheeze, exercise wheeze, breathlessness or night cough and demonstrable BHR are referred to in this paper as having symptomatic BHR.

Skin prick tests to 13 common allergens were performed. The allergens used are listed in Table 5. A drop of each allergen was placed on the forearm and the

skin pricked through the droplet. Excess fluid was blotted off immediately. After 15 minutes the largest diameter of the wheal and its perpendicular were recorded. Mean diameter was used in analyses. Skin test results for six children whose positive control was negative, or vice versa, were excluded from analyses.

Every tenth child studied was asked to provide from home a sample of house dust recently collected by vacuum cleaner. The samples, 59 from Wagga and 28 from Belmont, were stored at -20°C and examined for house dust mites.¹⁶

DATA PROCESSING

The data were coded and transferred to a Cyber 825 for analysis using the statistical package program SPSS. Chi-square tests were used to assess the significance of difference in prevalence rates of measured variables between the two populations.

RESULTS

The demographic details of the two populations are shown in Table 1. Although the age distribution in both towns was similar there was a slightly higher proportion of boys in the inland area. Children were considered to have life-long residence in the study town or in the same climactic area if they had not lived away from the area for more than six months. In both the inland and coastal areas, there was no difference in prevalence of respiratory symptoms, BHR or skin reactivity between those with and without life-long residence in their area.

Respiratory Illness

Table 2 shows that there was a trend for the four respiratory symptoms (wheezing, exercise wheezing,

TABLE 1 Comparison of children studied in inland and coastal populations.

		% of population	
		Inland	Coastal
Age	8 years	41	40
	9 years	44	49
	10 years	12	8
Sex	Male	54	51
	Female	46	49
Town of birth	Study	58	71
	Other	42	29
Life long residence	Study town	56	70
	Study area	66	86*
Total number		769	718

* $p < 0.05$ for the difference between populations.

TABLE 2 Comparison of the prevalence of respiratory symptoms in the two regions and their association with BHR.

	% of population with symptoms		% of symptomatic children with BHR	
	Inland	Coastal	Inland	Coastal
Wheezing	23.8	19.7	43.7	38.3
Exercise wheezing	11.9	6.8 [†]	59.3	54.3
Breathlessness	14.2	11.7	52.4	34.6*
Nocturnal cough	24.3	18.8 [†]	37.2	28.8
Any respiratory symptom	34.7	29.4*	36.7	29.9
Asthma diagnosed	13.0	9.1*	55.6	50.8
Asthma medicine ever used	13.9	10.2*	54.4	50.0
Hay fever	30.7	21.2 [†]	34.5	32.0
Eczema	22.5	21.2	31.8	21.9
Bronchitis under two years	23.7	21.1	29.7	26.5
Recent 'cold'	33.6	49.0 [‡]	29.1	16.5 [‡]
Total number	769	718		

* $p < 0.05$, [†] $p < 0.01$, [‡] $p < 0.001$ for the difference between populations.

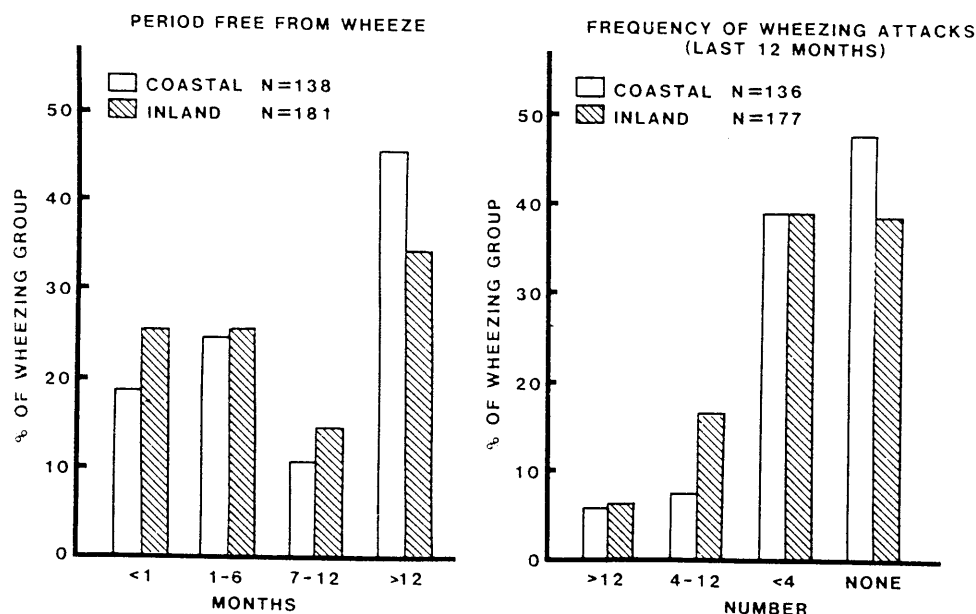


FIGURE 1 LHS: Percentage of children with a history of wheezing classified by the period free from wheeze for the two populations. RHS: Same children classified by the frequency of wheezing in the last 12 months.

breathlessness and night cough) to be more common inland. The differences were only significant for exercise wheeze and night cough. More inland children had symptoms when all four symptoms were considered together (35% v 29%, $p < 0.05$). Inland children with a history of wheezing were more likely to have had an attack of wheezing in the preceding 12 months (15% v 10%, $p < 0.01$) and these attacks were slightly more frequent. Of the children who reported wheeze, fewer

inland children had been free of attacks for more than 12 months (34% v 46%, $p < 0.01$). In both areas nearly 40% of the children who reported diagnosed asthma had not had an attack in the last 12 months, and the frequency of attacks and period free from asthma was similar in both areas (Figure 2).

The increased prevalence of diagnosed asthma inland was associated with a greater use of asthma medicine at any time (13% v 10%, $p < 0.05$), in the immediate past

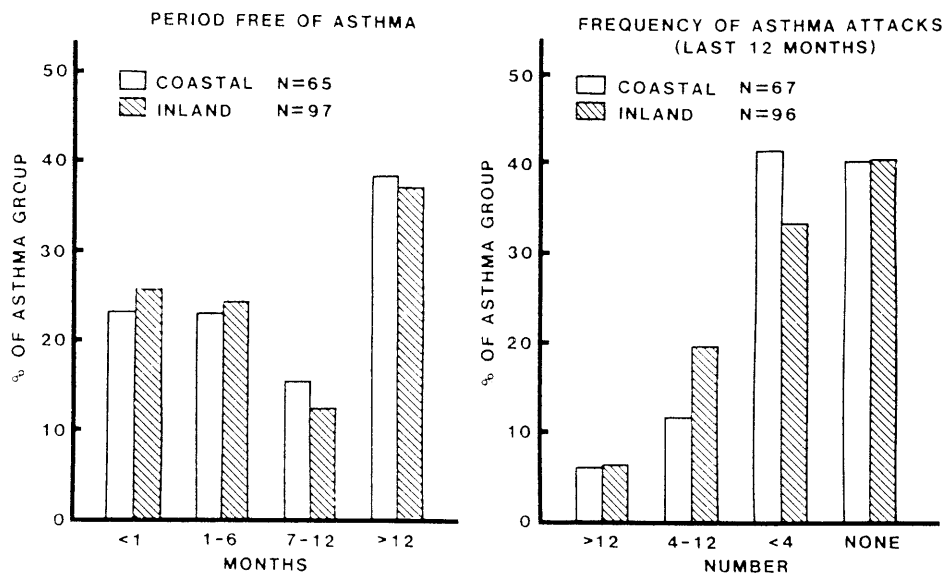


FIGURE 2 LHS: Percentage of children who had been diagnosed before the study as having asthma classified by the period free from asthma attacks for the two populations. RHS: Same children classified by the frequency of asthma attacks during the last 12 months.

12 months and on a daily basis (2.5% v 0.8%, $p < 0.05$). Hay fever was more common in the inland area but eczema was not.

A similar proportion of children in both areas had bronchitis diagnosed before the age of two years. Table 3 shows that paternal and maternal histories of asthma ($p < 0.05$) and hay fever ($p < 0.001$) were more common inland as was paternal eczema ($p < 0.01$).

Bronchial Hyperresponsiveness

There were differences in BHR between the two areas (Table 4). The prevalence of moderate to severe BHR was 12% inland and 9% in coastal children, increasing to 19% inland and 15% coastal ($p < 0.05$) for any BHR. Not all children with respiratory symptoms had BHR

(Table 1). However, when the two areas were compared, for each symptom there was a trend for a higher proportion of inland children to have BHR (Table 2). More inland children had symptomatic BHR (13% v 9%, $p < 0.05$) but the difference for moderate to severe symptomatic BHR was not significant (9% v 7%). The ratio of boys to girls with symptomatic BHR was 1.3 for the inland town and 1.5 for the coastal town.

TABLE 4 Comparison of prevalence of bronchial hyperresponsiveness and symptomatic BHR in the two regions.

	% of population	
	Inland	Coastal
Bronchial hyperresponsiveness		
Moderate and severe BHR	11.8	9.2
Mild BHR	7.0	5.7
All BHR	18.8	14.9*
Males	18.7	17.7
Females	19.0	11.7
Symptomatic BHR		
Moderate and severe BHR	8.8	6.7
Mild BHR	3.9	2.1
All BHR	12.7	8.8*
Males	14.2	10.6
Females	11.1	6.9
Total number	769	718

TABLE 3 Comparison of family history of associated illnesses in the two regions.

		% of population	
		Inland	Coastal
Asthma	Paternal	12.2	8.4*
	Maternal	15.1	10.7*
Hay fever	Paternal	31.5	17.2‡
	Maternal	42.1	29.4‡
Eczema	Paternal	6.8	4.2†
	Maternal	8.4	8.9
Total number		769	718

* $p < 0.05$, † $p < 0.01$, ‡ $p < 0.001$ for the difference between populations.

* $p < 0.05$ for the difference between populations.

TABLE 5 Comparison of prevalence of skin reactions to 13 allergens in children in both regions.

Allergens	% of population with atopy		% of atopic children with BHR		% of atopic children with symptomatic BHR	
	Inland	Coastal	Inland	Coastal	Inland	Coastal
House dust	12.1	19.5 [‡]	48.4	38.6	40.9	28.8
<i>D. farinae</i>	17.9	25.9 [‡]	45.7	29.6*	37.0	23.2*
<i>D. pteronyssinus</i>	11.3	20.3 [‡]	54.0	35.6*	42.5	28.3*
Cat	6.4	8.2	51.0	32.2	38.8	29.3
Dog	3.3	3.9	52.0	17.9*	40.0	17.9
Horse	8.3	7.0	50.0	34.0	40.6	26.5
Feathers	12.5	18.4 [‡]	47.9	33.3*	37.5	25.2
Ragweed	14.7	9.9 [†]	45.1	32.4	37.2	24.3
Timothy grass	25.5	12.4 [‡]	36.7	25.8	29.6	18.2*
Rye grass	24.7	10.9 [‡]	38.9	25.6	31.6	16.9*
Plantain	19.1	11.3 [‡]	44.9	30.9	37.4	22.5*
<i>Aspergillus</i>	11.3	6.7 [‡]	48.3	27.1*	39.1	17.0*
<i>Alternaria</i>	15.9	8.1 [‡]	50.0	22.4 [‡]	40.2	15.8 [†]
Any allergen	37.6	38.2	34.3	25.2*	26.3	18.3*
Total number	769	718				

* $p < 0.05$, $^{\dagger} p < 0.01$, $^{\ddagger} p < 0.001$ for the difference between populations.

Skin Allergy

In both areas 38% of children had a positive reaction to one or more of the allergens (Table 5). Inland children were more reactive to pollen extracts, especially timothy and rye grass. Coastal children were more reactive to extracts of house dust, the two common house dust mites and mixed feathers. The differences in

atopy were seen both in the number of children with a positive reaction and in the size of the wheals (Figures 3 and 4). Coastal children were more likely to have larger reactions to the house mite allergens and smaller reactions to the grass and weed pollens.

The relationship between skin allergy, respiratory symptoms and BHR in each population are compared

SKIN TEST REACTION TO HOUSE DUST MITES

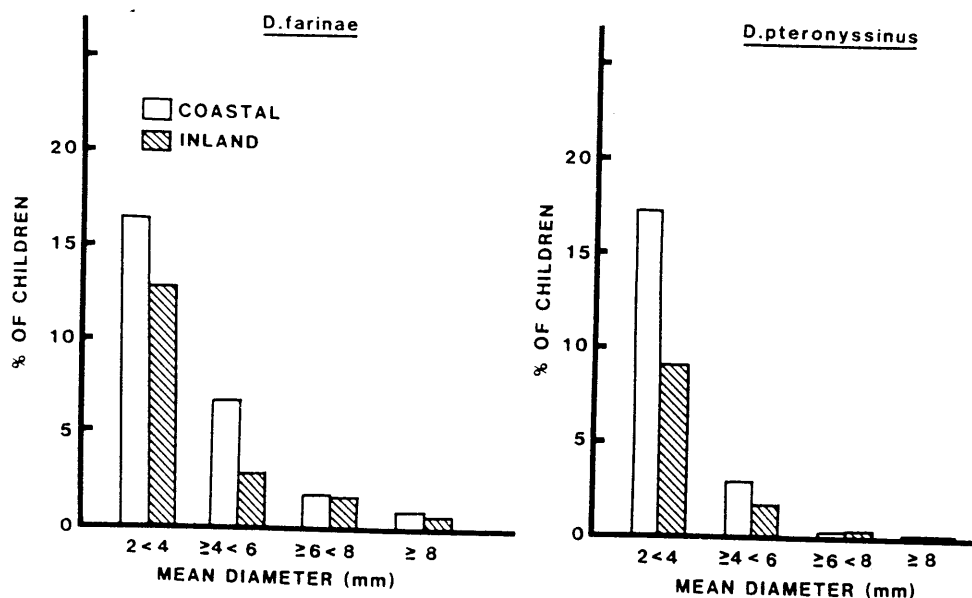


FIGURE 3 Percentage of children with skin test reactions to house dust mites according to size of reaction for the two populations.

SKIN TEST REACTION TO GRASS POLLENS

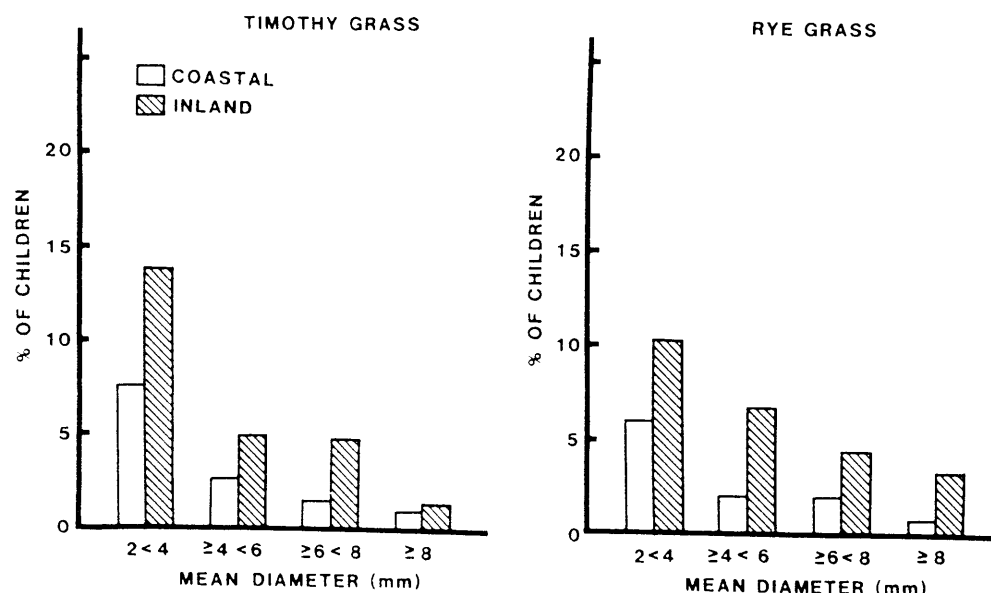


FIGURE 4 Percentage of children with skin test reactions to timothy and rye grasses classified according to size of reaction for the two populations.

in Table 5. A higher proportion of atopic children in the inland area had symptomatic BHR compared with the coastal population (26% v 18%, $p < 0.05$). This association was true for individual allergens. Symptomatic BHR was more common in atopic children in the inland area, whether they were reactive to *D. farinae* (37% v 23%, $p < 0.05$) or to timothy grass (30% v 18%, $p < 0.05$). However, in both areas, the majority of atopic children did not have symptomatic BHR and, conversely, of the children with BHR and symptoms, 22% of inland children and 21% of coastal children were not atopic.

House Dust Samples

The majority of samples from inland houses, where the climate is dry, were either devoid of house dust mites or contained very few. In addition to fewer samples being positive inland (15% v 95%), the mean mite count of samples was also lower (11/gm v 429/gm). Only *D. pterynissinus* was found inland whereas both *D. pterynissus* and *D. farinae* mites were found in dust collected from homes in the humid coastal region.

DISCUSSION

Previous studies to investigate the prevalence of asthma have relied on questionnaire data and/or the testing of lung function to define asthmatic groups in the popula-

tion.¹⁷⁻²¹ The additional measurement of BHR in this study further defines a subgroup within the spectrum of illnesses that present as wheezing in childhood.²² Clearly, not all children who reported a history of respiratory symptoms or diagnosed asthma had demonstrable BHR on the day they were tested. This could reflect either maturation²³ or the need for other provocative factors such as acute infection that are known to precipitate BHR.²⁴ Conversely, there also exists a small group of children with BHR but who have no history of diagnosed asthma or related respiratory symptoms. However, the combination of symptoms and BHR, both independently measured, permits the definition of a group of children whose significance approximates that of clinical asthma. In this study, the proportions of children with respiratory symptoms, BHR and symptomatic BHR were shown to be different in two regions with different patterns of atopy.

The proportion of coastal children who reported either wheezing or asthma was similar to that found in other studies in Australia,¹⁷⁻¹⁹ North America²⁰ and England.²⁴ However, the higher prevalence rates of all respiratory symptoms, including reported asthma and hay fever, that were found in the inland town more closely resembled those found in a study in New Zealand.²¹ The prevalence rates of both BHR and symptomatic BHR were also increased inland. The increased male-female ratio for symptomatic BHR in

both towns was consistent with the previously reported higher prevalence of asthma and wheezing in boys¹⁸ however there was no difference between the sexes for BHR alone. The slight excess of boys in the inland sample did not account for all the increased prevalence of symptomatic BHR in the inland sample.

Possible factors that may contribute towards a higher prevalence of symptomatic BHR include respiratory infection, seasonal changes in aeroallergens and a genetic predisposition. Bronchitis before the age of two years had a similar prevalence in both towns however recent respiratory infection was higher in the coastal region and did not account for the difference in BHR prevalence that was found. There were no seasonal differences between the towns since the two studies were undertaken in June when there is neither high humidity in the coastal town nor high pollen counts in the inland town. There was a higher frequency of maternal and paternal history of asthma and hay fever inland suggesting that children in this area may have had a greater genetic predisposition to asthma. It is unlikely that established asthmatics have migrated selectively to Wagga Wagga. Rather, the greater frequency of reported asthma and hay fever in young to middle-aged adults is more likely to be due to the same environmental factors accounting for excess asthma among their children. The obvious one is exposure to higher concentrations of pollens.

Although the proportion of children with a positive skin test reaction to any of the allergens was similar in both study towns, skin reactivity to grass pollens was twice as frequent inland and dust mite reactivity predominated on the coast. The higher frequency of skin reactivity to *D. farinae* than to *D. pteronyssinus* in both groups has been noted previously in clinical studies in Australia (unpublished data). Although *D. farinae* had not been isolated previously from samples of house dust in Australia, this mite was found in a number of the specimens from the coastal town.¹⁶ The difference in skin reactivity between the two regions may be due to both the presence of specific allergens in the environment and the degree of exposure. In inland Australia, the lack of humidity probably accounts for the low prevalence of dust mites.²⁵ Moreover, in this area there is greater exposure to aeroallergens resulting from extensive pastures and crop agriculture.

The higher prevalence of BHR and symptoms in the town with pollen rather than mite aeroallergens, decreases the likelihood that allergy to house dust mites is the major single factor initiating BHR. Rather, if the predisposition to BHR is present, the prevalence of symptomatic BHR moves in parallel with the total burden of aeroallergen.

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REFERENCES

- 1 Broder I, Higgins M W, Matthews K P, Keller J B. Epidemiology of asthma and allergic rhinitis in a total community. Tecumseh, Michigan. *J Clin Immunol* 1974; 53: 127-38.
- 2 Bryant D H, Burns M W. The relationship between bronchial hyperreactivity and atopic status. *Clin Allergy* 1976; 6: 373-81.
- 3 Morrison Smith J, Harding C K, Cumming G. The changing prevalence of asthma in schoolchildren. *Clin Allergy* 1971; 1: 57-61.
- 4 Martin A J, Landau L I, Phelan P D. Natural history of allergy in asthmatic children followed to adult life. *Med J Aust* 1981; 2: 470-4.
- 5 Hendrick D J, Davies R J, d'Souza M F, Pepys J. An analysis of skin test reaction in 656 asthmatic patients. *Thorax* 1975; 30: 2-8.
- 6 Barber R A, Telowitz M D, Thompson H C, Burrows B. Immediate skin test reactivity in a general population sample. *Ann Int Med* 1976; 84: 129-33.
- 7 Burrows B, Telowitz M D, Barber R A. Respiratory disorders and allergic skin test reactions. *Am Int Med* 1976; 84: 134-9.
- 8 Godfrey R C, Griffiths M. The prevalence of immediate positive skin tests to *Dermatophagoides pteronyssinus* and grass pollen in school children. *Clin Allergy* 1976; 6: 79-82.
- 9 Morrison Smith J. Skin tests and atopic allergy in children. *Clin Allergy* 1973; 3: 269-75.
- 10 Bryant D H, Burns M W. Bronchial histamine reactivity; its relationship to the reactivity of the bronchi to allergens. *Clin Allergy* 1976; 6: 523-32.
- 11 Woolcock A J, Colman M H, Jones M W. Atopy and bronchial reactivity in Australian and Melanesian populations. *Clin Allergy* 1978; 8: 155-64.
- 12 Nathan R A, Kinsman R A, Spector S L, Horton D J. Relationship between airways response to allergens and nonspecific bronchial reactivity. *J Allergy Clin Immunol* 1979; 64: 491-9.
- 13 McAllen M K, Asseum E S K, Maunsell K. Housedust mite asthma. *Brit Med J* 1970; 2: 501-4.
- 14 Cochran W G, Cox G M. Experimental designs. Wiley, New York, 2nd ed, 1957.
- 15 Yan K, Salome C, Woolcock A J. Rapid method for measurement of bronchial hyperresponsiveness. *Thorax* 1983; 38: 760-5.
- 16 Green W. The house dust mite, *Dermatophagoides farinae*, in Australia. *Med J Aust* 1983; 2: 259-60.
- 17 Williams H, McNicol K N. Prevalence, natural history and relationship of wheezy bronchitis and asthma in children. *Brit Med J* 1969; 4: 321-4.
- 18 Peat J K, Woolcock A J, Leeder S R, Blackburn C R B. Asthma and bronchitis in Sydney schoolchildren. 1. Prevalence during a six year study. *Am J Epidemiol* 1980; 111: 721-7.
- 19 Mitchell C, Miles J. Lower respiratory tract symptoms in Queensland schoolchildren. The questionnaire: its reliability and validity. *Aust NZ J Med* 1983; 13: 264-9.
- 20 Dodge R R, Burrows B. The prevalence and incidence of asthma and

- asthma-like symptoms in a general population. *Am Rev Resp Dis* 1980; **122**: 567-75.
- ²¹ Sears M R, Jones D T, Silva P A, Simpson A, Williams M W. Asthma in seven year old children: a report from the Dunedin Multidisciplinary Child Development Study. *NZ Med J* 1982; **95**: 533-6.
- ²² Lee D A, Winslow N R, Speight A N P, Hey E N. Prevalence and spectrum of asthma in childhood. *Brit Med J* 1983; **286**: 1253-8.
- ²³ Martin A J, McLennan L A, Landau L I, Phelan P D. The natural history of childhood asthma to adult life. *Brit Med J* 1980; **1**: 1397-1400.
- ²⁴ Empey D W, Laitinen L A, Jacobs L, Gold W M, Nadel J A. Mechanisms of bronchial hyperreactivity in normal subjects after upper respiratory tract infection. *Am Rev Resp Dis* 1976; **113**: 131-9.
- ²⁵ Spielsma F Th M, Zuideme P, Leupon M J. High altitude and house dust mites. *Brit Med J* 1971; **1**: 82-4.

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