Eur Respir J, 1993, 6, 662–669
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European Respiratory Journal
ISSN 0903 - 1936

Predictive nature of bronchial responsiveness and respiratory symptoms in a one year cohort study of Sydney schoolchildren

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Predictive nature of bronchial responsiveness and respiratory symptoms in a one year cohort study of Sydney schoolchildren. J.K. Peat, B.G. Toelle, C.M. Salome, A.J. Woolcock. ©ERS Journals Ltd 1993.

ABSTRACT: We wanted to examine the predictive nature, over one year, of bronchial hyperresponsiveness (BHR) and recent wheeze (in the previous 12 months), which are the measurements frequently used to classify asthma for epidemiology.

A prospective cohort study of 236 children, aged 8–11 yrs, was undertaken, with an initial baseline study, followed by four studies at three monthly intervals over one year. At each study, we measured bronchial responsiveness to histamine by the rapid method, respiratory symptoms by parent questionnaire, and atopy by skin prick tests to common allergens. Airflometer readings, which are closely related to FEV_1, were self-recorded. Baseline data were used to classify children into the four categories of "current asthma" (BHR and wheeze), "wheeze only", "BHR only", or "normal".

During the year following baseline study, the group initially classified as "wheeze only" had normal Airflometer variability, and 59% had wheeze, and 33% had BHR, which tended to be mild. In the group initially classified as "BHR only", 52% had wheeze with a peak in winter, and 62% had BHR during the following year. This group had more severe bronchial responsiveness and Airflometer variability than the normal and wheeze only groups. The group initially classified as current asthma had a more severe condition, with continued BHR (100%), and wheeze (93%), increased Airflometer variability and more atopy. Thus, the natural history of bronchial responsiveness, respiratory symptoms and allergic history in this group was different from the other three groups.

We conclude that the definition of "current asthma" as BHR plus recent wheeze discriminates the group with an ongoing significant abnormality in terms of respiratory impairment and, as such, is clearly important for epidemiological studies which require an objective measurement of asthma that has clinical importance.
Eur Respir J., 1993, 6, 662–669.

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Keywords: Airflometer variability
asthma
atopy
bronchial hyperresponsiveness
children
respiratory symptoms

Received: August 20 1992
Accepted after revision February 25 1993

The natural history of asthma in childhood is poorly documented, largely because the inherently variable nature of asthma makes it a particularly difficult disease to classify in populations. In the absence of a gold standard, the definition of "current asthma" which we have found most useful for epidemiology, and which has been used by other research groups, is the presence of bronchial hyperresponsiveness (BHR) plus a report of wheeze in the previous 12 months [1–5]. This definition classifies the group with an objective measure of airway abnormality, with recent symptoms of asthma severe enough to be reported, and with a more severe impairment both in terms of physiological and of clinical characteristics [6]. However, the predictive power of this classification is not known. Because both BHR and wheeze are subject to variations with time and season [7–11], the classification is likely to be subject to concurrent variations.

In 1988, we collected baseline data from a cohort of children, who we stratified according to the wheeze and BHR criteria which we commonly use to classify asthma severity for epidemiology [1–3, 6]. In the following year, part of the cohort was studied on four occasions at three monthly intervals. At each study, information on recent respiratory symptoms and on bronchial responsiveness to histamine was collected and, in addition, children self-recorded Airflometer readings for a two week period. In this paper, we report the predictive nature of wheeze and BHR for childhood respiratory illness over the following year.

Methods

Population

In spring (November) 1988, a random cross-section of 440 children, aged 8–10 yrs, living in Villawood, a western suburb of Sydney, was enrolled in a study of asthma and allergy [12]. At the time of enrolment,

parents were asked for permission for children to continue in studies conducted in the summer, autumn, winter and spring of the following year. At each follow-up, data of bronchial responsiveness, atopy, questionnaires and Airflometer readings were collected. A total of 270 children enrolled, of whom 236 completed the study.

Bronchial responsiveness

A histamine bronchial challenge test was administered using the rapid method [13]. Forced expiratory manoeuvres were measured by Vitalograph dry spirometer, and were repeated until two readings of forced expiratory volume in one second (FEV_1) within 100 ml of one another were obtained, of which the largest FEV_1 value was used in analyses. Subjects who had taken a beta-agonist within 6 h, or theophylline within 12 h, of presenting for testing were asked to withhold medication before being tested next day. Histamine diphosphate was administered by DeVilbiss No. 45 hand-held nebulizer, in doses ranging from 0.03–7.8 μmol histamine. The test was stopped if the FEV_1 fell by 20% or more, or if all histamine dose steps to 7.8 μmol had been administered. Salbutamol aerosol was administered to aid recovery, when necessary.

A dose-response curve was obtained for each subject with a fall of 20% or more, by plotting the percentage change in FEV_1 from the post-saline (control) value against the logarithm of the dose of histamine. For subjects who experienced a fall of 20% or more, the dose of histamine that caused a 20% fall in FEV_1 ($PD_{20}FEV_1$) was interpolated. Subjects with a $PD_{20}FEV_1$ were classified as having BHR. Dose-response ratio (DRR) was calculated for all subjects as the percentage fall in FEV_1 at last dose, divided by the total dose administered [14]. Many subjects had an FEV_1 which remained stable, or improved slightly, during bronchial challenge, and thus gave a zero or negative DRR value, so that a constant of 3 was added to all DRR values in order to obtain a positive value for logarithmic conversion [15]. DRR values are, therefore, indicated by units: (% fall FEV_1/μmol)+3. One subject who had an FEV_1 less than 60% predicted was excluded from bronchial challenge tests, and was found to have 5% reversibility when given bronchodilator. This child, who was in the normal group, was considered to have missing data for that study in analyses.

Respiratory symptoms and medication use

Information on recent respiratory symptoms was collected by a parent completed questionnaire, which asked whether the child had had wheeze, exercise wheeze, or night cough, or had used any medicine for asthma, in the three month period since the last study [1]. Children with a report of wheeze or exercise wheeze in the previous three months were classified as having "recent wheeze" for that follow-up period. Similarly, children who had used asthma medicine in the previous three months were classified as having "recent medication" for that follow-up study.

Atopy

Because skin prick tests have good repeatability [16], only data from the first follow-up study in summer 1989 were used. Atopy was measured by skin prick tests to the forearm [17]. The allergens tested were house-dust mites (*Dermatophagoides pteronyssinus* and *D. farinae*), cat dander, pollens (rye grass and plantain) and the mould, *Alternaria tenuis*. Histamine and glycerol were used as positive and negative controls. After 15 min, wheal size was recorded as the long axis and its perpendicular, mean wheal size was used in analyses. A skin prick reaction was regarded as positive if the wheal size was 3 mm or more. The small number of children with a negative histamine or a positive glycerol response were retested, and were excluded from analyses if the result was maintained. Atopy was defined as one or more positive reactions. Children were considered sensitized to house-dust mites or pollens if they had a positive reaction to either of the allergens in the group.

Airflometer variability

Each child was shown how to use an Airflometer (Glaxo Pty Ltd, Australia) and, prior to the recording period, had their technique checked by a nurse. The Airflometer is an impeller device, that measures expiratory flow in arbitrary units closely related to FEV_1 [18]. Children were asked to record the highest of three attempts to obtain a maximum Airflometer value. Values were recorded twice daily, for a two week period following bronchial challenge testing. Children using bronchodilators were asked to record Airflometer measurements both before and 10 min after medication. Airflometer variability *i.e.* the variation in readings, was calculated for each day with complete data as amplitude percentage (highest minus the lowest reading as a percentage of highest [19]). Mean daily Airflometer variability was used in analyses.

Statistical methods

Data were analysed using the statistical package SAS (SAS Institute Inc., Cary, NC, USA). DRR and PD_{20} FEV_1 values were converted to base 10 logarithms, and geometric mean values are reported. Prevalence rates and mean values are reported with the 95% confidence interval (CI). Chi-squared was used to determine the significance of differences in categorical variables. Chi squared trend statistic was used to determine the significance of seasonal trends in categorical variables. Repeat-ed measures analysis of variance was used to determine the significance of the differences between continuous variables and trends with time. Unadjusted odds ratios, that is odds ratios for symptoms or BHR in the presence of sensitivity to a specific allergen, and calculated without taking account of sensitivity to other allergens, were calculated using the Mantel-Haenzel technique. Logistic regression was used to compute adjusted odds ratios for the risk of

children having wheeze and/or BHR in the presence of one sensitivity to one allergen, adjusted for positive sensitivity to the other allergens tested.

Definitions

Children were classified into wheeze/BHR groups using their 1988 baseline data only. The group with BHR and with wheeze in the previous 12 months when initially studied were classified as "current asthma". The group with BHR but no wheeze in the previous 12 months when initially studied were classified as "BHR only". The group with wheeze in the previous 12 months but no BHR when initially studied were classified as "wheeze only". All other children were classified as being in the "normal" group. At follow-up studies, children with a DRR value above 9.2% fall FEV_1/μmol+3, that is children above the 97.5th percentile of DRR among a large random sample of lifetime asymptomatic children [15], were classified as having an abnormal DRR value. Normal values for Airflometer variability are not available, but the 97.5th percentile in the normal group in this study was 28%. We therefore used a slightly more conservative cut-off point of 30% or more to classify children as having abnormal Airflometer variability.

Table 1. – Prevalence of wheeze, medication used and diagnosed asthma in children who continued in the study, compared with children who did not continue in the follow-up cohort

	Continued in study	Lost to follow-up
Total number	270	170
Wheeze ever	24 (21.1–31.6)	25 (18.2–31.2)
Wheeze in last year	16 (11.9–20.7)	18 (12.0–23.4)
Medicine in last year	15 (11.0–19.6)	19 (12.9–24.7)
Diagnosed asthma	18 (13.6–22.8)	21 (14.5–26.7)

Data are presented as percentage and 95% confidence interval in parenthesis.

Results

Of 440 children, aged 8–11 yrs, with baseline data collected in 1988, 270 undertook to attend follow-up study in 1989. Table 1 shows that the respiratory illness history of those who continued in the study was not significantly different from that of children who opted not to take part. Only the data from 236 children who attended all four follow-up studies in 1989 are reported.

The percentage of study children who had recent wheeze and BHR each season, and their mean DRR and Airflometer variability is shown in table 2. The numbers vary because the proportion of children who failed to return a questionnaire each season ranged from 6% in the summer to 13% in the winter. The prevalence of recent wheeze rose slightly at the winter study, but the trend did not quite reach significance ($p<0.1$). The prevalence of BHR did not change significantly during the study period from the prevalence of 15.3% (95% CI 10.7–19.9) measured at baseline. Mean DRR and Airflometer variability did not change significantly either.

In the study cohort, 173 children were classified as normal, 27 as wheeze only, 21 as BHR only, and 15 as current asthma, according to initial baseline measurements. The percentage of children with doctor diagnosed asthma was 8% of the "normal group"; 52% of the "wheeze only" group; 14% of the "BHR only" group, and 87% of the "current asthma" group. There were 16 children (7% of the sample) who were using a preventive asthma medication, *i.e.* inhaled corticosteroid or sodium cromoglycate, of whom two were in the normal group, four were in the wheeze only group, and the remaining 10 were in the current asthma group. Table 3 shows the percentage of children in each group who had characteristics associated with asthma illness at any of the four follow-up studies. The conditions of BHR or an abnormal DRR value were more group-dependent than the conditions of wheeze or asthma medication use. The group initially classified as BHR only was intermediate between the wheeze only and current asthma groups, both in terms of bronchial responsiveness and abnormal Airflometer variability.

Table 2. – Prevalence of measured characteristics each season in the total sample studied

	Summer	Autumn	Winter	Spring
BHR				
%	13	13	16	17
95% CI	(8.9–17.5)	(8.9–17.5)	(11.5–20.9)	(12.6–22.3)
n	235	235	235	235
Dose-response ratio				
Mean	4.1	3.9	4.2	4.2
95% CI	(3.9–4.4)	(3.6–4.1)	(3.9–4.4)	(3.9–4.5)
n	235	235	235	235
Recent wheeze				
%	15	18	22	17
95% CI	(10.5–19.7)	(13.2–23.0)	(17.1–27.7)	(11.9–21.4)
n	232	227	183	187
Airflometer variability				
Mean	12.8	13.4	13.1	13.2
95% CI	(11.7–14.0)	(12.0–14.8)	(11.9–14.3)	(12.1–14.3)
n	187	173	194	209

BHR: bronchial hyperresponsiveness; 95% CI: 95% confidence interval.

Table 3. – Percentage of each group which had any of the listed characteristics at any time during the four follow-up periods

	Classification at initial study				
	Normal	Wheeze only	BHR only	Current asthma	p value*
Subjects n	173	27	21	15	
BHR	17	33	62	100	<0.001
Abnormal DRR	1	0	24	73	<0.001
Recent wheeze	18	59	52	93	<0.001
Recent medicine	5	18	10	20	<0.05
Abnormal Airflometer variability	6	7	9	47	<0.001

*: the difference between groups. BHR: bronchial hyperresponsiveness; DRR: dose-response ratio.

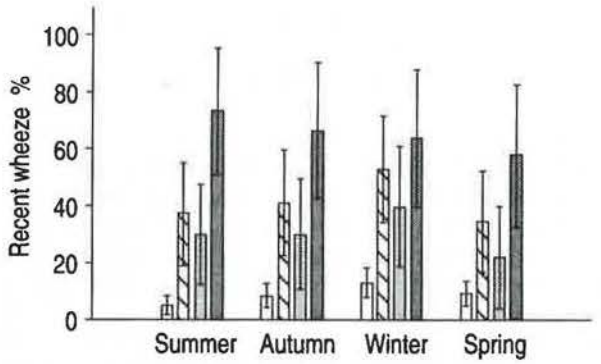

Fig. 1. – Prevalence of recent wheeze each season in children classified according to baseline data. The bars are the 95% confidence interval for each group. □: normal; ▭: wheeze only; ▨: BHR only; ■: current asthma. BHR: bronchial hyperresponsiveness.

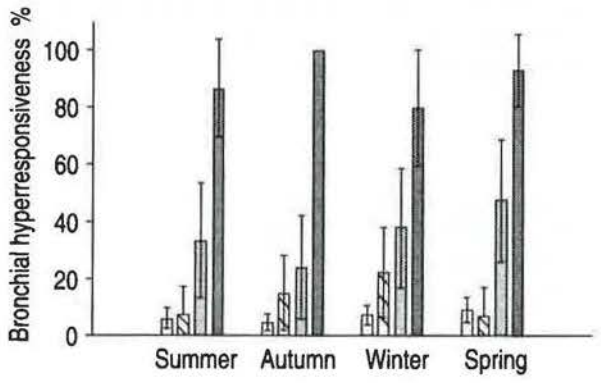

Fig. 2. – Prevalence of bronchial hyperresponsiveness each season in children classified according to baseline data. The bars are the 95% confidence interval for each group. □ : normal; ▭ : wheeze only; ▨ : BHR only; ■: current asthma. BHR: bronchial hyperresponsiveness.

The percentage in each group with recent wheeze each season is shown in figure 1. The group initially classified as normals had a low rate of recent wheeze at each follow-up. Approximately 20–50% of children initially classified as wheeze only, or as BHR only, had recent wheeze at each of the following studies. In both groups, the prevalence of wheeze was highest in winter, but this slight seasonal peak did not constitute a significant trend. At all studies, the group initially classified as current asthma had significantly more symptoms than the other groups, with 60–70% reporting recent wheeze each season.

The percentage of children with BHR each season is shown in figure 2. The prevalence of BHR was very low in the group initially classified as normals. The group initially classified as wheeze only had a low rate of BHR each season, with a small peak in winter, with a trend that almost reached significance ($p<0.1$). Between 30–50% of the group initially classified as BHR only had BHR each following season, with a small, nonsignificant peak in spring. The group initially classified as current asthma had significantly more BHR each season than the other groups ($p<0.001$), and most children in this group retained their BHR each season.

There was an expected significant difference in DRR ($F=89.7$, $DF=233,3$, $p<0.001$) between groups, but repeated measures analysis did not indicate a time/group difference ($F=0.93$, $DF=699,9$; $p=0.5$). Figure 3 shows that the mean DRR in the group initially classified as wheeze only remained much the same as the normal group.

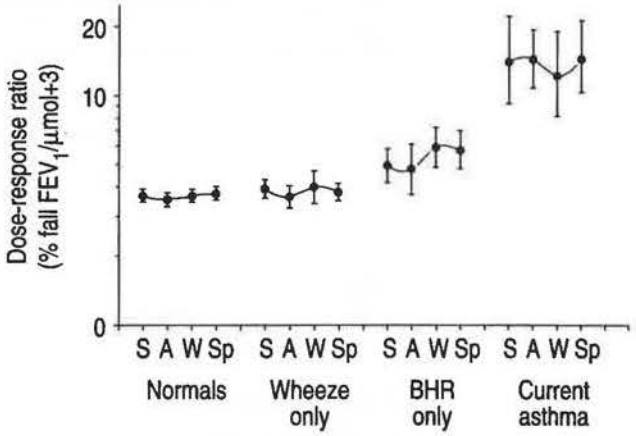

Fig. 3. – Mean dose response ratio in children classified according to baseline data. The points represent data collected in summer (S), autumn (A), winter (W) and spring (Sp). The bars are the 95% confidence intervals. FEV_1: forced expiratory volume in one second; BHR: bronchial hypperresponsiveness.

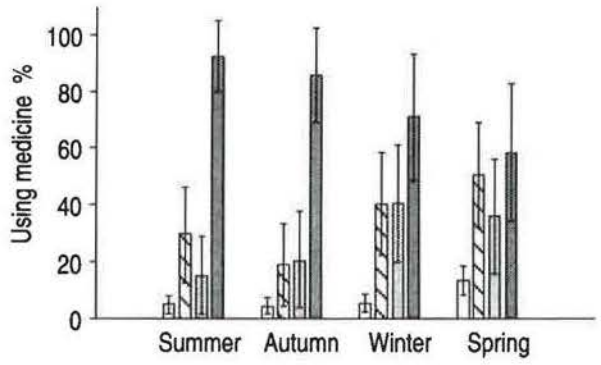

Fig. 4. – Prevalence of asthma medication use each season in children classified according to baseline data. The bars are the 95% confidence interval for each group. □: normal; ▨: wheeze only; ▩: bronchial hyperresponsiveness only; ■: current asthma.

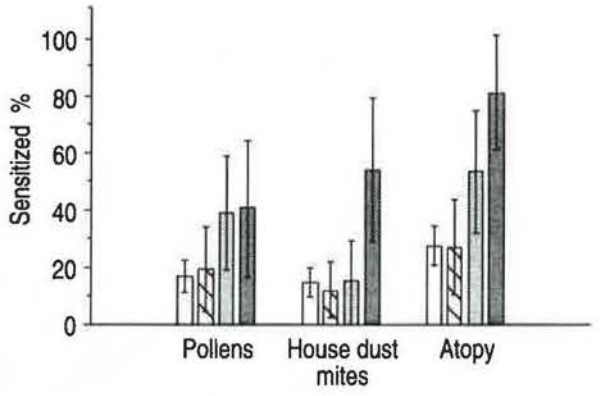

Fig. 5. – Prevalence of atopy and of sensitization to pollens or house-dust mites at the summer follow-up in children classified according to baseline data. The bars represent 95% confidence intervals. □: normal; ▨: wheeze only; ▩: bronchial hyperresponsiveness only; ■: current asthma.

The group initially classified as BHR only had responsiveness which continued at all studies as intermediate between the current asthma and wheeze only groups. The current asthma group had more severe responsiveness than the other groups throughout ($p<0.001$). Mean Airflometer values (data not included) were more variable than DRR values, but showed the same relative between-group variations.

The rate of use of any medicine for asthma (preventive medication or bronchodilator) each season is shown in figure 4, and tended to follow the same pattern as recent wheeze. Almost all of the current asthma group used an asthma medicine each season, but the proportion declined as the study progressed. The rate of asthma medicine use was lower in the other groups in summer and autumn, but increased in winter and spring, when all groups, except the normal group, had an equal rate of use of asthma medicines.

The percentage of children who were atopic, or who were sensitized to pollens or house-dust mites, is shown in figure 5. Almost 80% of the group initially classified as current asthma were atopic, which was significantly higher than the other groups ($p<0.001$), and this group also had more house-dust mite sensitivity ($p<0.001$). The prevalence of pollen sensitivity in the groups initially classified as current asthma or BHR only was similarly high, and was significantly higher than the other groups ($p<0.01$). No children initially classified as BHR only or wheeze only groups were sensitized to pets, and only one child in each group was sensitized to moulds. The unadjusted and adjusted odds ratio for being in the wheeze only, BHR only, or current asthma groups if sensitized to specific allergens is shown in table 4. Pollen sensitivity was a significant risk factor for children having BHR only, and both pollen and house-dust mite sensitivity were significant risk factors for children having current asthma.

Table 4. – Unadjusted and adjusted odds ratios (and 95% confidence intervals) for children having "wheeze only", "BHR only" or "current asthma" in the presence of sensitivity to specific allergens

	Unadjusted odds ratio	Adjusted odds ratio	p value
Wheeze only			
Pollens	1.2 (0.4, 3.4)	2.1 (0.7, 6.8)	0.25
House-dust mites	0.8 (0.3, 2.9)	0.4 (0.1, 2.0)	0.25
BHR only			
Pollens	3.2 (1.3, 8.3)	3.9 (1.3, 11.6)	<0.02
House-dust mites	1.0 (0.3, 3.9)	0.7 (0.2, 2.7)	0.56
Current asthma			
Pollens	3.5 (1.2, 10.2)	1.3 (0.3, 5.5)	0.72
House-dust mites	7.1 (2.4, 20.2)	6.9 (2.0, 24.1)	<0.01
Pets	13.2 (2.0, 79.9)	14.2 (0.8, 242.7)	0.06
Moulds	5.2 (1.2, 27.9)	1.0 (0.1, 12.2)	0.97

BHR: bronchial hyperresponsiveness.

Discussion

In this study, we examined the predictive value, over one year, of epidemiological definitions of current asthma, based both on BHR and on recent symptoms of wheeze. In doing so, we found that the group that we initially defined as "current asthma" continued at follow-up as the group with the most severe ongoing illness, whereas the children initially classified as "wheeze only" or "BHR only" had relatively trivial conditions, with episodic symptoms and mild BHR, both of which showed small seasonal variations. The group initially classified as BHR only, had more sensitivity to pollens and slightly increased Airflometer variability, but the wheeze only group could not be discriminated from the "normals" by any characteristic other than their symptoms. On the other hand, children initially classified as current asthma had continual BHR and symptoms, and also had increased Airflometer variability and more atopy. These findings strengthen the value of our definition of current asthma for epidemiological studies in which an objective method is required for classifying the group with the most severe ongoing illness.

We used reliable methods to measure respiratory symptoms, atopy and bronchial responsiveness [1, 12, 16]. The questionnaire items that we used are reliable [1], and measurements of DRR have good repeatability when used for field studies of children [12]. We included Airflometer variability as a further measure of asthma severity which has recognized clinical validity. We chose Airflometers in preference to peak flow meters, because they are more sensitive, and the readings correlate closely with peak expiratory flow rate [18]. We encountered some problems in achieving long-term compliance in this largely healthy sample, in that the consent rate for baseline study was 58% and, despite many reminders and regular incentives, 13% of enrolled children did not complete, and a small number of children failed to return all Airflometer charts or questionnaires. However, the characteristics of the sample cohort were not significantly different from those of the children who did not continue in the study. Because the primary aim was to follow-up variations in BHR and symptoms with time, potential sampling bias was not a major problem. The stratified groups were large enough to give adequate statistical power to detect clinically meaningful within-subject changes in bronchial responsiveness (a doubling dose change in $PD_{20}FEV_1$) in repeated measures analyses. Our reported percentages of BHR and wheeze do not represent population prevalence rates, but they were not significantly different from those found previously in a large random sample in the same area [3]. It is unlikely that many children were misclassified because regular use of preventive medication had returned symptoms and BHR to the normal range. In the follow-up cohort, most children using preventive medicine were in the current asthma group. Only three children in each of the normal and wheeze only groups were using a preventive medication and may have been misclassified.

The natural history of BHR and symptoms throughout childhood is poorly documented and, because longitudinal studies in children have generally been limited to small, select groups [20, 21], the short-term variability of symptoms and BHR in children with less severe illness is not known. There are inherent problems in studying children with BHR because this group cannot be detected by questionnaire and can only be identified by screening whole populations, using bronchial challenge tests. By enrolling a population sample, our follow-up cohort comprised a relatively small number of children with BHR and/or wheeze, and a larger group of normals. However, use of DRR rather than $PD_{20}FEV_1$ values overcame some of the limitations encountered by other researchers [9, 20], because a value indicating the severity of the bronchial responsiveness was obtained for all subjects [15]. In this study, the group initially classified as BHR only had a severity of both bronchial responsiveness and Airflometer variability intermediate between the normal and current asthma groups and, as such, had a more severe condition than children initially classified as wheeze only.

Two of the most important risk factors for current asthma in children are sensitivity to house-dust mite and pollen allergens [16, 22, 23]. Pollens show large seasonal fluctuations, and house-dust mite allergen levels may similarly fluctuate where there is a cold season. There is growing evidence that exacerbations of asthma symptoms occur in response to sudden large increases in airborne allergens [24, 25]. In the USA, increased hospital asthma admissions and asthma mortality have been associated with pollen atopy [11, 26]. Similarly, studies of clinic attenders show that both BHR and symptoms can increase during the ragweed season in sensitized subjects [27]. The hypothesis that increased BHR in children can result from pollen-induced airway inflammation [10] is supported by the finding of increased BHR in pollen allergic adults [28]. In our cohort, symptoms did not increase in spring in any group, even the group initially classified as BHR only which had a higher prevalence of pollen sensitivity and slightly increased BHR in spring. We were not able to obtain pollen counts, but it is possible that pollens were not the most important allergens in the region, or that our studies were too widely spaced to detect a short-term peak in bronchial responsiveness.

Childhood wheeze is a common condition, which has been reported to have occurred in up to 40% of children in this study region [3]. However, it is thought that many symptoms of wheeze in children are trivial, in that they probably relate to airway size rather than to a clinically important respiratory illness. In this study, we found no evidence that children in the wheeze only group had a condition associated with an important impairment. In terms of Airflometer variability and severity of bronchial responsiveness, this group was most similar to the normal group. The only difference was that children in this group had mild BHR and symptoms in winter, which may have occurred in response to viral infections or to other transient environmental factors [29].

In contrast, the current asthma group were more allergic to house-dust mites, and had more severe bronchial responsiveness than the other groups. There is a close association between ongoing asthma morbidity and atopy

in children [20], and there is growing evidence that continual exposure to house-dust mite allergens cumulatively increases bronchial responsiveness [30]. Other, large population studies show that house-dust mite allergy is closely associated with current asthma in children, and has a more important association with childhood BHR than does sensitivity to pollens [16, 22, 23]. A clinic study of asthma patients in Sydney found that house-dust mite and cat dander sensitivity were associated with BHR, but that pollen sensitivity was not important [31]. In Virginia, USA, where house-dust mite levels are much lower, but seasonal variations are more marked, house-dust mite allergic patients have increased symptoms when allergen levels are high [32]. In Sydney, house-dust mite allergen levels are above the suggested threshold for sensitization all year round [33], and the significant risk of current asthma in children atopic to house-dust mites is consistent with the findings from large random cross-sectional samples [6, 16, 23].

The use of BHR in an operational definition of asthma for epidemiology has obvious advantages over the more subjective measurements, such as the presence of a doctor's diagnosis of asthma. The importance of international and regional comparisons to investigate the aetiology of asthma is widely-recognized and, for such studies, an objective measurement which reflects severity is essential. A doctor's diagnosis does provide recognition of disease severity and, in this study, the majority of the current asthma group had been labelled as having asthma by a doctor and, because of this, were using an asthma medicine. However, a diagnosis of asthma in conjunction with recent symptoms of wheeze did not discriminate groups in terms of abnormal Airflometer variability (Chi-squared=7.1, DF=3, NS), or medication requirement (Chi-squared=7.5, DF=3, NS) suggesting that this definition is less able to identify the group with a current and severe abnormality. Our question of diagnosis referred to any time in the past, and this would also have limited its power to discriminate the group with a current, severe respiratory illness.

In summary, the natural history of asthma has been difficult to describe, particularly because asthma is characterized by variable symptoms and physiological characteristics at all ages. By studying stratified groups, we have shown that measurements of wheeze and BHR can be used to classify population samples of children according to ongoing severity. In particular, we found that our definition of current asthma classified the group with the most chronic and severe condition. Because longitudinal data show that children with more severe BHR tend to maintain their condition as they become older [34], this is the group in which asthma is most likely to have important sequelae. The finding that this group has a chronic impaired condition is important for epidemiological studies of the prevalence and aetiology of asthma, in which it is necessary to discriminate the group with the most severe, ongoing impairment.

Acknowledgements: The authors thank the National Health and Medical Research Council of Australia, the Asthma Foundation of NSW, the Bankstown City Council, the Health Department of NSW, and the Community Health and Anti-Tuberculosis Association for funding this project. In addition, they thank the New South Wales Department of Education, and all parents and children for their support and co-operation.

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