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# Factors associated with bronchial hyperresponsiveness in Australian adults and children

J.K. Peat, C.M. Salome, A.J. Woolcock

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**ABSTRACT: To accurately assess putative risk factors for bronchial hyperresponsiveness (BHR), we have used multivariate models to analyse data from 4,366 children living in four regions and from 878 adults. A standard protocol was used to measure bronchial responsiveness to histamine.**

**The prevalence of BHR was high at 7–9 yrs (16–18%), decreased significantly at 11–14 yrs (7–8%), and then increased in adults (12–14%). Atopy was the most important risk factor for BHR at all ages. In children, parental asthma, early respiratory illness and being born in Australia also had a significant influence, and eating fish more than once a week had a protective effect. No effect of parental smoking, gender or race was found. In adults, BHR was associated with being female and with smoking history.**

**It appears that many factors have a significant influence on the presence of BHR, with environmental factors, particularly atopy, birthplace and diet, being the most important.**

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Department of Medicine, University of Sydney, NSW, Australia.

Correspondence: A.J. Woolcock
Institute of Respiratory Medicine
Royal Prince Alfred Hospital
Camperdown
NSW 2050
Australia

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In the last decade, population studies of asthma have focused on the measurement of bronchial hyperresponsiveness (BHR), because it is the single, objective measure of airway abnormality that is strongly associated with a clinical diagnosis of asthma [1, 2]. Although the measurement lacks sensitivity and, to a lesser extent, specificity as a marker of asthma [3], it has proved to be a useful indicator of the severity of current disease that is independent of diagnostic patterns and symptom awareness. Because there are both regional and racial differences in the prevalence of BHR, which relate to differences in the prevalence of respiratory symptoms [4–7], the study of BHR in populations is likely to provide objective evidence for the aetiology of asthma and, as such, has an important role. To interpret and compare measurements of BHR between populations, the factors that influence its distribution must be known. There have been few large population studies that have used multivariate modelling analyses to document the independent effects of such factors with precision.

We have measured the distribution of BHR in four population samples of children living in different regions of Australia, and in one population sample of adults. The data were collected during a series of studies designed to document the prevalence of BHR and its relationship to respiratory symptoms. In this paper, we report the relationship of BHR to atopy, age and sex. In addition, we examine the influence of early respiratory illness, race, country of birth, dietary fish, parental smoking and a parental history of asthma on the prevalence of BHR in children, and the influence of smoking history on the prevalence of BHR in adults.

## Methods

Four samples of children and one sample of adults were studied. Three samples of children were from New South Wales. The fourth sample of children and the sample of adults lived in Western Australia. Informed consent was obtained from parents of all children enroled and from all adult subjects. The samples and the methods of data collection have been reported in detail previously [8–11] and are summarized briefly below.

### *Populations*

The study regions in New South Wales were: Wagga Wagga, a rural town in the southwestern plains; Belmont, a coastal suburb of Newcastle; and Villawood, a western suburb of metropolitan Sydney. The Wagga Wagga and Belmont studies were conducted from 1982–1984; the Villawood study was conducted in 1986. At each study, a large random cross-section of 3rd and 4th grade schoolchildren, aged 7–10 yrs, was sampled. In Villawood, 5th grade

children aged 11 yrs were also included. The consent rate for study was 88% in Belmont, 83% in Wagga Wagga and 68% in Villawood. In Western Australia, adult subjects were drawn from a sample attending a community health survey in Busselton, a coastal town 250 km south of Perth. In 1981, 3,940 adults from approximately 6,000 living in the town attended, of whom one in four was randomly assigned to our study. A total of 1,170 adults was studied, of whom 922 were randomly selected on the basis of age, sex and socioeconomic status, in order to match the sample to the demographic characteristics of the population. In 1983, 1,293 children were also surveyed at their schools. Every second child of the first 400 tested was selected into our study, after which all children were selected.

### *Questionnaire and interview information*

Each child returned a parent-completed questionnaire with demographic information and details of respiratory history. The question of early respiratory illness was, "Was your child treated by a doctor or at a hospital for bronchitis before the age of two?" and the questions of parental asthma were, "Has the child's natural father (mother) ever had asthma?" with the options of answering "No" or "Yes". The question of diet was, "How often does your child eat a meal that contains fish?", with options of answering the following: rarely; once a month; once a week; more than once a week. Children who had a fish meal more than once a week were categorized as having "regular fish meals". The questions of parental smoking were, "Since the child was born did the father (mother) smoke at any time?" and "If yes, how many cigarettes each day does the father (mother) smoke now?". Country of birth was measured by the question, "Where was the child born?" and race was assessed at interview on the basis of visual characteristics.

In adults, details of smoking habit were collected by a self-administered questionnaire. Nonsmokers were defined as subjects who had never smoked regularly (one or more cigarettes a day). Ex-smokers were subjects who were nonsmokers when studied but who had reported previous regular smoking. Smokers were subjects who reported regular current smoking at the time of the 1981 study.

### *Bronchial responsiveness*

Each subject underwent a bronchial challenge conducted using the rapid method [12]. Forced expiratory manoeuvres were measured by Vitalograph dry spirometer and were repeated until two tracings reproducible to 100 ml were obtained, of which the larger was used to calculate forced expiratory volume in one second ($FEV_1$) and forced vital capacity (FVC). Subjects who had taken a beta-sympathomimetic aerosol within 6 h, or theophylline compounds within 12 h, of presenting for testing were not studied that day but were asked to withhold medication before returning for testing the next day. Subjects who had an $FEV_1$ <60% of predicted were excluded from having a bronchial challenge test. The test was conducted by administering histamine diphosphate in doses ranging from 0.03–3.9 μmol histamine by DeVilbiss No. 40 hand-held nebulizer, using solutions of 3.1, 6.2, 25 and 50 $mg \cdot ml^{-1}$. Following bronchial challenge, salbutamol aerosol was administered to aid recovery when necessary.

The challenge was stopped if there was a fall in $FEV_1$ ≥20% or if all histamine dose steps to 3.9 μmol had been administered. Children with a fall in $FEV_1$ of 10–19% after 3.9 μmol of histamine had been given were administered a further dose to a total of 7.8 μmol. Subjects who experienced an $FEV_1$ fall of ≥20% were, classified as having BHR. Adults with >15% fall in $FEV_1$ at 3.9 μmol histamine, when the challenge was stopped, were also categorized as having BHR.

Our own research team conducted all studies using the same equipment. Although some of the observers varied at each study, all were taught how to administer the protocol to a set standard by senior personnel. Nebulizers, of known output, were rigorously checked for correct functioning prior to and during each challenge.

### *Atopy*

Atopy was measured by skin prick test reactions to a panel of common allergens, applied to the forearm [13]. The seven common allergens tested at all locations were: house dust mites (*Dermatophagoides pteronyssinus*, and *D. farinae*), cat dander, rye grass, plantain and moulds (*Alternaria tenuis* and *Aspergillus fumigatus*). In Wagga Wagga, Belmont and Villawood, house dust, dog and horse danders, feather mix, ragweed and timothy grass allergens were also tested. In Busselton children, sorghum, orchard, barley, veldt and timothy grasses, dog dander and capeweed allergens were tested. In adults, cattle dander, barley grass, couch grass, orchard grass, wild oats, capeweed and peppermint tree allergens were tested. Fifteen minutes after application of allergens, wheal size was recorded as the mean of the long axis and its perpendicular. Atopy was defined as one or more positive skin prick test reactions with a mean size of at least 3 mm in children or 4 mm in adults [14, 15].

### *Statistical methods*

Data were analysed using the statistical package program SAS [SAS Institute Inc., Cary, NC, USA]. Ranges for prevalence figures are those of the 95% confidence interval (CI). Chi-squared analyses of

contingency tables were used to determine the significance of the association between categorical variables and the Mantel Haenzel statistic, to calculate unadjusted odds ratios for BHR. Logistic regression was used to assess the likelihood of variables being independently associated with BHR, and to determine adjusted odds ratios and their 95% confidence intervals.

## Results

The sample sizes and ages of subjects included in analyses are shown in table 1. In Belmont and Wagga Wagga, the samples were limited to 7–10 yr old children; in Villawood, 11 yr old children were also included. In these samples, all 7 yr old children were within a month of turning 8 yrs. The Busselton samples comprised 6–14 yr old children and all ages of adults. Seven children who were excluded from bronchial challenge because of abnormally low lung function were regarded as having BHR [8]. Fifty five adults with abnormally low lung function were excluded from analyses [9, 16].

A total of 4,366 children and 878 adults had complete data. The prevalence of BHR in each sample, and the percentage of subjects with the characteristics which were considered as risk factors for BHR, are shown in table 2. In children, the prevalence of BHR was 19.6% in Wagga Wagga, which was significantly higher than the other three regions where the prevalence in the same age group of 7–10 yrs ranged from 15–15.8% ($p<0.001$). The prevalence of atopy was similar in all samples of children and slightly higher in adults.

The distribution of BHR by age in all samples combined is shown in figure 1. In children, the prevalence was highest at 7–10 yrs (16–18%), after which it declined sharply. Between 11–14 yrs, the prevalence of BHR was low (7–9%) and appeared to remain stable. In adults, the data has been aggregated in 10 yr age groups because of small numbers at some ages. The prevalence of BHR was 12–14% and remained at this level until late adulthood.

Table 1. – Number and age of subjects studied in each area

| | Age yrs | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | Total |
| **Childhood studies** | | | | | | | | | | |
| Belmont | - | 42 | 384 | 387 | 180 | - | - | - | - | 993 |
| Wagga Wagga | - | 35 | 510 | 629 | 197 | - | - | - | - | 1371 |
| Villawood | - | 30 | 394 | 402 | 257 | 134 | - | - | - | 1217 |
| Busselton | 42 | 103 | 118 | 109 | 117 | 112 | 74 | 62 | 148 | 885 |

| | Age yrs | | | | | | |
|---|---|---|---|---|---|---|---|
| | 20–29 | 30–39 | 40–49 | 50–59 | 60–69 | 70–79 | Total |
| **Adult study** | | | | | | | |
| Busselton | 138 | 175 | 151 | 166 | 177 | 109 | 916 |
| Number with BHR measured | 138 | 173 | 146 | 156 | 160 | 95 | 868 |

BHR: bronchial hyperresponsiveness.

Table 2. – Prevalence of bronchial hyperresponsiveness (BHR) and potential risk factors in children and adults studied in each area and Busselton adults

| | Belmont | Wagga Wagga | Villawood | Busselton Children | | Busselton Adults |
|---|---|---|---|---|---|---|
| Total n | 993 | 1371 | 1217 | 447 | 438 | 868 |
| Age yrs | 7–10 | 7–10 | 7–12 | 7–10 | 11–14 | 20–88 |
| BHR prevalence % | 15.8 | 19.6 | 15.3 | 15.0 | 8.4 | 12.9 |
| 95% CI | 13.5–18.1 | 17.5–21.7 | 13.3–17.3 | 11.7–18.3 | 5.8–11.0 | 10.7–15.1 |
| Atopy | 31.1 | 33.3 | 29.8 | 34.7 | | 42.7 |
| Parental asthma | 17.7 | 22.8 | 15.5 | 17.8 | | NI |
| Early respiratory illness | 21.3 | 24.2 | 20.0 | 13.5 | | NI |
| Gender % male | 53.8 | 52.4 | 48.4 | 53.8 | | 49.9 |
| Born outside Australia | NI | NI | 23.7 | 11.5 | | NI |
| Regular fish meals | NI | NI | 8.4 | NI | | NI |
| Mother current smoker* | NI | NI | 21.5 | NI | | NI |
| Parent smoker# | NI | NI | 67.3 | NI | | NI |
| Subject current smoker** | NI | NI | NI | NI | | 27.6 |

95% CI: 95% confidence interval; NI: no information collected; *: ≥10 cigarettes·day$^{-1}$; #: either parent had smoked since child was born; **: subject smoking ≥10 cigarettes·day$^{-1}$.

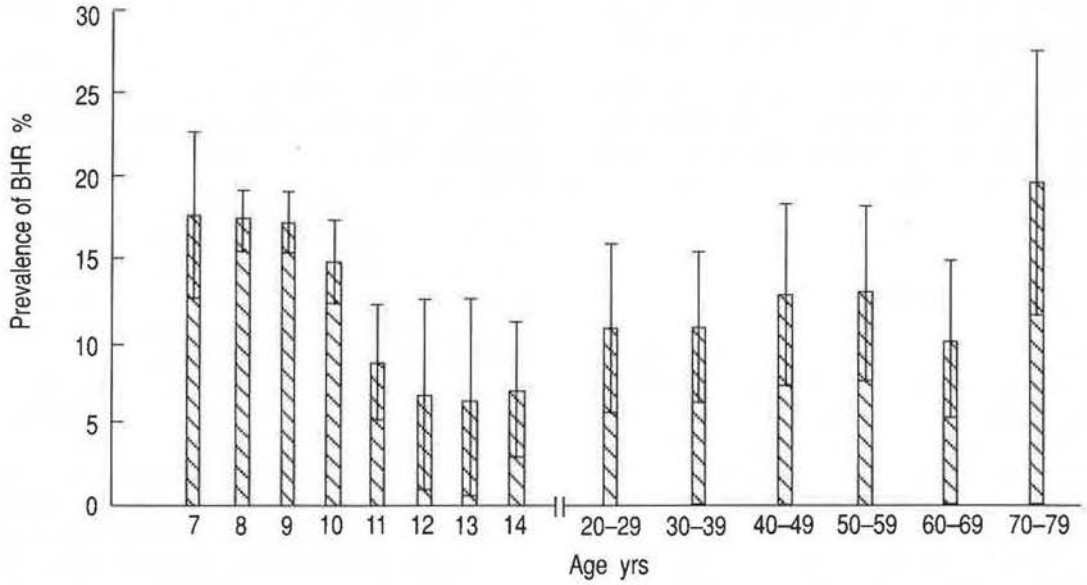


Fig. 1. – Prevalence (%) of bronchial hyperresponsiveness (BHR) by age group in 4,366 children (all areas combined) and in 868 adults.

The distribution of BHR by gender is shown in figure 2. In univariate analyses, there appeared to be slightly more BHR in males <14 yrs of age when all data were combined (17.3 *vs* 14.4%, p<0.05) but the difference was not significant when any age group was considered separately. In adults, there was a reversal of the gender difference with significantly more BHR in females than in males (15.2 *vs* 10.1%, p<0.01).

The associations of potential risk factors with BHR in children in the combined Wagga Wagga, Belmont and Villawood samples are shown in table 3. Because atopy, parental asthma and early respiratory illness may act either as confounders or as intervening variables (because all three factors may be related to region), unadjusted odds ratios were also calculated. These showed an increased risk of BHR in Wagga Wagga. However, in the multivariate model, there was no significant effect of gender or of region on the prevalence of BHR. We also investigated risks stratified by the presence of recent wheeze. In the 594 children with recent wheeze (16.6% of the sample), all factors except early respiratory illness remained significant: atopy (OR=3.94, 95% CI 2.82–5.49, p<0.001); parental asthma (OR=1.55, 95% CI 1.11–2.17, p<0.02); male gender (OR 1.38, 95% CI 0.99–1.92, p=0.07). In children with no recent wheeze, all factors except gender remained significant: atopy (OR=2.29, 95% CI 1.79–2.90, p<0.001); parental asthma (OR=1.57, 95% CI 1.19–2.06, p<0.01); early respiratory illness (OR=1.68, 95% CI 1.28–2.21, p<0.001).

Questions about parental smoking, country of birth and frequency of fish meals were only included in the questionnaire to Villawood children. The relative importance of these factors is shown in table 4.

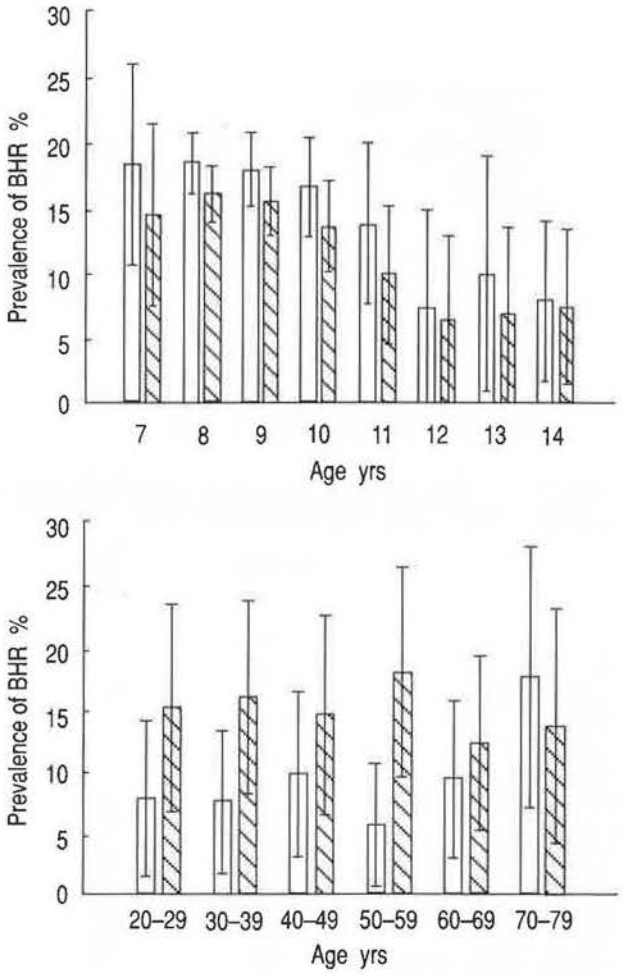


Fig. 2. – Prevalence (%) of bronchial hyperresponsiveness (BHR) by gender in 4,366 children (all areas combined) and in 868 adults. □ : males; ▨: females.

Table 3. – Significance of potential risk factors for bronchial hyperresponsiveness in 3,581 children living in three areas of New South Wales

| Factor | Unadjusted odds ratio (95% CI) | p value* | Adjusted odds ratio (95% CI)** | p value* |
|---|---|---|---|---|
| Atopy | 3.50 (2.92–4.18) | <0.001 | 3.38 (3.07–3.72) | <0.001 |
| Parental asthma | 2.34 (1.93–2.85) | <0.001 | 1.95 (1.58–2.40) | <0.001 |
| Early respiratory illness | 2.27 (1.88–2.75) | <0.001 | 2.14 (1.76–2.62) | <0.001 |
| Gender male | 1.20 (1.01–1.43) | <0.05 | 1.11 (0.92–1.34) | NS |
| Compared to Belmont: | | | | |
| Living in Wagga Wagga | 1.30 (1.05–1.61) | <0.05 | 1.21 (0.97–1.52) | NS |
| Living in Villawood | 0.96 (0.76–1.21) | NS | 0.98 (0.80–1.29) | NS |

*: NS: not significant at the p<0.05 level; **: likelihood ratio for model=35.2, df=41, p=0.72; 95% CI: 95% confidence interval.

Table 4. – Significance of potential risk factors for bronchial hyperresponsiveness in children living in Villawood, New South Wales and Busselton, Western Australia

| Factor | Villawood | | Villawood & Busselton | |
|---|---|---|---|---|
| | Adjusted odds ratio (95% CI)** | p value* | Adjusted odds ratio (95% CI)# | p value* |
| Total number | 1217 | | 2102 | |
| Atopy | 4.78 (3.4–6.7) | <0.001 | 6.10 (4.6–8.1) | <0.001 |
| Parental asthma | 2.27 (1.5–3.4) | <0.001 | 1.90 (1.4–2.6) | <0.001 |
| Early respiratory illness | 1.42 (0.9–2.1) | <0.08 | 1.68 (1.2–2.3) | <0.01 |
| Born outside Australia | 0.56 (0.4–0.9) | <0.03 | 0.63 (0.5–0.9) | <0.003 |
| Regular fish meals | 0.35 (0.1–0.9) | <0.04 | - | |
| Age >11 yrs | NI | | 0.49 (0.3–0.7) | <0.001 |
| Gender male | 1.09 (0.7–1.5) | NS | 1.03 (0.7–1.4) | NS |
| Race Asian descent | 0.77 (0.4–1.5) | NS | | |
| Birthplace × atopy | 0.48 (0.1–2.6) | NS | NI | |
| Birthplace × fish meals | 1.19 (0.1–8.3) | NS | NI | |
| Parental smoking | - | NS | NI | |

*: NS: not significant at the p<0.1 level; **: likelihood ratio for model=31.5, df=40, p=0.83; #: likelihood ratio for model=51.2, df=55, p=0.62; NI: no information collected; 95% CI: 95% confidence interval.

Being born outside Australia and eating fish more than once a week both had a significant protective effect against BHR. The prevalence of BHR was 17.6% in children born in Australia and 16.2% in irregular (once a week or less) and non-fish eaters compared with 8.0% in children born outside Australia and 4.9% in regular fish eaters. In this sample, 30% of children were non-fish eaters, 62% ate fish once a week or less and 8% ate fish regularly. No significant interactions between birthplace and atopy or fish diet were found (p>0.2 and p>0.9, respectively) and the effect of race (Asian/non-Asian descent) was not significant. Logistic regression confirmed the age effect seen in univariate analyses (table 4). Only data from Villawood and Busselton children were included because of the wider age range in these samples. There was a significant reduction in BHR after the age of 11 yrs and after other significant factors were taken into account.

In children, the effect of parental smoking was investigated but no association with BHR was found. The data for parents' smoking habit were tested as both categorical and continuous variables. Logistic regression showed that there was no association between BHR and number of cigarettes·day$^{-1}$ smoked by the mother (p>0.8). In univariate analyses, no relationship was found between BHR and parental smoking categorized as smoking ≥10 cigarettes·day$^{-1}$ by either parent (p>0.7); smoking ≥20 cigarettes·day$^{-1}$ by either parent (p>0.8); smoking ever by either parent (p>0.7); smoking ≥10 cigarettes·day$^{-1}$ by the mother (p>0.3); smoking ≥20 cigarettes·day$^{-1}$ by the mother (p>0.9); or smoking ever by the mother (p>0.7).

The independent effects of factors considered as risk factors for BHR in adults are shown in table 5. As in children, atopy was the strongest factor. In adults, gender (being female), age (being >70 yrs), and smoking history (both current and past smoking) were also important factors. A significant interaction was found between atopy and age (p<0.02), indicating a decrease in the effect of atopy on BHR with increasing age. There was no interaction between atopy and smoking (p=0.21).

Table 5. – Significance of potential risk factors for bronchial hyperresponsiveness in 868 adults living in Busselton, Western Australia

| Factor | Unadjusted odds ratio (95% CI) | p value | Adjusted odds ratio (95% CI)* | p value |
|---|---|---|---|---|
| Atopy | 2.45 (1.61–3.68) | <0.001 | 2.59 (1.71–3.90) | <0.001 |
| Gender female | 1.82 (1.20–2.74) | <0.01 | 2.14 (1.39–3.29) | <0.001 |
| Age >70 yrs | 1.61 (0.93–2.88) | NS | 3.54 (1.64–7.67) | <0.01 |
| Current smoker | 1.45 (0.91–2.36) | NS | 1.88 (1.13–3.12) | <0.02 |
| Ex-smoker | 1.50 (0.82–2.88) | NS | 2.05 (1.03–4.08) | <0.04 |

NS: nonsignificant; 95% CI: 95% confidence interval; *: likelihood ratio for model=22.4, df=18, p=0.22.

## Discussion

We have documented both the prevalence of BHR to histamine and the adjusted odds ratios for the factors which affect it in children and adults. Atopy to common allergens and age are the most important independent predictors of BHR. In adults, smoking history and gender (being female) were also important. In children, a parental history of asthma and respiratory infection in the first 2 yrs of life had a significant influence on BHR and, after taking these factors into account, being born outside Australia and regular fish meals both had a protective effect against BHR. We did not find a significant effect of parental smoking, race (Caucasian/Asian), gender or region (coastal/inland).

Because our own research group collected all data using standard methods, we were able to combine data and obtain large sample sizes in order to determine the relative importance of risk factors for BHR with good precision. For children, random samples were selected in each region, so that the reported distributions of BHR are likely to reflect those of the populations from which the samples were drawn. A high consent rate for study was obtained in the Belmont and Wagga Wagga samples (83–88%). Although the consent rate in Villawood was lower (68%), a survey of non-attenders found no bias in terms of asthmatic symptoms [10]. No accurate figures were collected for Busselton children but the consent rate was thought adequate [11], and prevalence rates obtained from that sample are probably reliable. The adult sample in Busselton was basically one of volunteer attenders but 66% of the population attended and, in demographic terms, the sample was representative of the general population. Elimination of subjects unsuitable for bronchial challenge because of poor resting lung function may have led us to underestimate the effects of some factors, particularly atopy and cigarette smoking associated with severe asthma and chronic airflow limitation, respectively.

The rapid method for measuring bronchial responsiveness is reliable [9, 17] and has better reproducibility than other methods suitable for field use [18]. Slight differences in the protocol for administering the final dose of histamine were unlikely to have had more than a minimal effect on the correct categorization of BHR. The proportion of adults falsely classified as BHR negative would have been extremely small, and in children was <2% [8]. Also, because the majority of atopic subjects react to a few common allergens [19], differences in allergen panels used in each region would have had a very small effect on the prevalence of atopy. The size of Busselton and Villawood samples precluded the meaningful assessment of risk factors for BHR stratified by symptom history in those groups but stratification of data from the combined groups of children showed that the importance of risk factors was generally maintained, especially for parental asthma and atopy, and was not unduly influenced by symptomatic children.

These studies have allowed us to document the distribution of BHR in a wide age range of subjects. The prevalence of BHR was highest at age 7–9 yrs and then declined to approximately half the rate at 11–14 yrs, after which it rose slightly to remain fairly stable until late adulthood. Because of consistency in methodology, the low rate of BHR in late childhood was unlikely to be due to artefact but there are no population studies with a full age range for comparison. A high prevalence of BHR in childhood, with a lower rate in adults, has been reported in a selected population [20]. BURNEY *et al.* [21] studied a population sample of 511 adults and found little change in prevalence of BHR in nonsmokers, but increasing prevalence in BHR with age in smokers. CERVERI *et al.* [22] found no correlation between BHR and age between 15–65 yrs, although the sample was selected. The decrease in BHR that we found in late childhood is consistent with remission from symptoms at this age [23]. It appears that BHR decreases considerably at this age and increases again in early adulthood, although a study of these age groups is needed to confirm this. The natural history of BHR is poorly documented but longitudinal data show that it is the children with more severe BHR who are more likely to have continuing BHR in later years [24].

The extent to which changes in BHR with age reflect normal changes in bronchial tone of the airways as they grow, or loss of elastic recoil and progressive airway disease in later life, is not known. Increased BHR in childhood may result from the physical size of the airways or greater airway lability. It is possible that smaller airways result in a proportionately greater loss of $FEV_1$ during bronchial challenge or a greater deposition of histamine in the large airways [20].

In children, smoking is not a confounder and BHR is rarely associated with illness other than asthma. However, in adults, an increase in the prevalence of BHR in older age groups is likely to relate to an increase in diseases other than asthma, including smoking-related conditions [16, 25]. We found that smoking habit was an important predictor of BHR. A significant association between BHR and cigarette smoking, especially in older age groups and in atopic smokers, has also been documented by other researchers [26, 27]. The prevalence of regular smoking was relatively low in the adults studied, suggesting that regular health survey interventions had decreased smoking prevalence in this community or that smokers may have been more reluctant to attend.

In children, we found slightly more BHR in males in univariate analyses, which is consistent with an excess of respiratory symptoms in males at this age. However, the difference was not significant after adjusting for other factors, so that the variability normally assigned to gender is probably due to other factors, particularly atopy, which have a differential gender distribution. In adults, the prevalence of BHR was consistently higher in females at all ages and was unlikely to be due to artefact. Other studies have also found more BHR in adult females [22, 28, 29], although BURNEY *et al.* [21] reported slightly more BHR in adult males (16 *vs* 12%).

The current analyses confirm that, at all ages, atopy is the most important known risk factor for BHR. A close association between atopy and BHR has been established in earlier studies both by our group [4, 9, 14] and by other researchers [30, 31]. The current analyses confirm the strong independent effect of atopy after taking account of other factors. Although the importance of atopy is widely recognized and suggests a strong role of local allergens in respiratory illness, it is not known whether atopy and BHR develop simultaneously or whether a causal relationship exists. It is clear that the effect of atopy is most important in early childhood [14], decreases with age [10] and that house dust mite atopy has a particularly important role [19].

In these studies, early respiratory illness and a parental history of asthma appear to be significant risk factors for BHR. In terms of the relationship with early respiratory illness, we cannot be certain that parents of children with BHR do not preferentially report early symptoms in their child. Also, the extent to which early illness is associated with a viral infection is not known and its relationship with BHR in later life is not conclusively established [32]. However, such a relationship may result from the early illness predisposing children to later BHR by triggering causal mechanisms, or because the illness is an early expression of increased responsiveness [33]. The role of parental asthma is more clearly established and is likely to have a genetic component although a common environmental mechanism cannot be ruled out. CLIFFORD *et al.* [34] report an increased risk for BHR in univariate analyses of approximately 1.5 in children of asthmatic parents, which is similar to our estimate.

In Villawood children, eating fish regularly seemed to have a significant protective effect against BHR, which was independent of race and country of birth. The effect appeared to be a threshold effect, since the prevalence of BHR in children who ate fish irregularly or not at all was similar, but further information of this needs to be collected. There has been interest in the therapeutic value of fish oils because dietary enrichment with fish oil lipids can alter patterns of cellular mediators [35]. However, in a group of asthmatics studied in the clinic, addition of fish oil lipids to the diet appeared to suppress neutrophil function but did not improve symptoms or severity of BHR [36, 37]. The questions of fish meals that we used were not specific, in that we did not ask about the type of fish or the quantity eaten, for how long fish had been regularly included in the child's diet or whether other foods, such as red meats, were excluded. But, because of the theoretical evidence that fish lipids should improve asthma, this finding deserves further investigation in a study specifically designed to test the hypothesis that fish oil can reduce BHR.

There is growing concern about the effects of parental smoking on the respiratory health of children but we found no evidence that parental smoking increased the risk of BHR. This is contrary to a body of evidence for an increased risk in children of smoking parents, especially those with mothers who smoke and those who are >11 yrs of age [38–41]. We only collected information of parental smoking from children <12 yrs but no suggestion of an association was seen. Although we had a relatively low consent rate in the sample in which we measured parental smoking, the prevalence of parents who had ever smoked was high, at 67%, making a preferential consent by nonsmoking parents unlikely but our results may have been influenced by many children having been exposed to tobacco smoke at some time in their lives.

It is thought that differences in the prevalence of BHR between countries and races [5, 6] result from a combination of genetic and environmental influences. Our finding that children born in Australia had a higher prevalence of BHR, adjusted for other factors including race, than children born in other countries raises some interesting questions. The Villawood region, from which one of our samples was drawn, includes a community of Asian migrants. Because race was not a risk factor for BHR in these populations, there is reduced possibility that genetic factors are predominant and an increased possibility that BHR has a largely environmental aetiology. Children born in Australia may be exposed to an additional allergen load that is most effective in causing BHR early in life, but this hypothesis remains to be tested.

The presence of BHR is obviously influenced by a variety of genetic, physiological and environmental risk factors of which atopy remains the most important

known factor in both adults and children. This, taken with the evidence of a higher prevalence of BHR in children born in Australia and a lower prevalence in children on a "protective" diet, suggests that environmental influences are very important. It is vital that future epidemiological studies collect information on both BHR and asthma from populations living in regions with markedly different environments, for which the risk factors can be measured accurately. Such investigations are likely to provide invaluable insights into the aetiology and prevention of asthma.

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