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Perception of respiratory symptoms after methacholine-induced bronchoconstriction in a general population

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Perception of respiratory symptoms after methacholine-induced bronchoconstriction in a general population. G. Devereux, D.J. Hendrick, S.C. Stenton. ©ERS Journals Ltd 1998.
ABSTRACT: In an epidemiological study, methacholine-induced bronchoconstriction was used as a physical illustration of the sensations associated with asthma. The objective of this study was to assess whether familiarity with these sensations could be used as a measure of asthma prevalence.

Eight hundred and seventy six subjects aged 20–44 yrs completed a respiratory questionnaire and a measurement of airway responsiveness (the provocative dose of methacholine causing a 20% fall in forced expiratory volume in one second (PD_{20})). Subjects were asked about their perception of, familiarity with and description of the respiratory sensations experienced at the time of maximal bronchoconstriction.

The questionnaire-derived lifetime prevalences of wheeze, chest tightness and undue breathlessness were 43, 35 and 22% respectively. Asthma medication was used by 8% and the lifetime prevalence of diagnosed asthma was 12%. Quantifiable levels of airway responsiveness were measured in 34%, and airway responsiveness in the range considered to be consistent with untreated active asthma was present in 21%. Bronchoconstriction was perceived by 59%. Perception of bronchoconstriction was associated with the magnitude of bronchoconstriction, younger age, female sex and questionnaire-reported symptoms. Of subjects able to perceive bronchoconstriction, 58% reported previous experience of (familiarity with) the associated respiratory sensations. Familiarity with the sensations of bronchoconstriction was associated with questionnaire-reported symptoms, diagnosed asthma and increasing levels of airway responsiveness. There was poor agreement between the respiratory symptoms reported by questionnaire before the methacholine test and the words used to describe respiratory sensations induced by the test.

Familiarity with the sensations of methacholine-induced bronchoconstriction has all the appropriate associations of a measure of asthma prevalence and may be a useful adjunct to symptom questionnaires and airway responsiveness measurements in epidemiological studies. A sizeable number of subjects can be identified with intermediate levels of airway responsiveness, who are able to perceive bronchoconstriction and are familiar with the sensations associated with it, yet who are not recognized to suffer from asthma.
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The identification of asthma in epidemiological studies is beset by a number of methodological problems [1, 2]. Respiratory symptom questionnaires are convenient to administer, but the data obtained are subjective and can be influenced by the presence of other cardiorespiratory disorders, the respondents' level of comprehension, memory, self image, concerns, smoking habit and psychological profile [3–6]. Records of an established clinical diagnosis of asthma depend on patients' willingness to report symptoms and physicians' interpretation of them, and can be influenced by sex, socioeconomic status and diagnostic fashion [7, 8]. Measurements of ventilatory function may not demonstrate airway obstruction, and when they do, they may not be able to distinguish an asthmatic cause from one attributable to other diseases [9, 10].

Measurements of airway responsiveness are objective and repeatable, and, within populations, correlate with other measures of asthma activity such as symptoms and use of medication [11–14]. However, high levels of airway responsiveness are not specific to asthma, and are found in other conditions associated with reduced ventilatory function. Furthermore, airway responsiveness measurements are unimodally distributed in the general population, and there is no clear level above which asthma can be said to be unequivocally present and below which it can be said to be absent [15, 16].

In a previous study of shipyard workers, it was noted that subjects with high levels of airway responsiveness did not report more respiratory symptoms on a questionnaire than those with low levels. However, when bronchoconstricted during a methacholine test, those with high levels of airway responsiveness were more likely to report previous experience of the associated sensations [17]. Airway responsiveness measurements, thus, appeared to be a better guide to previous experience of substantial bronchoconstriction (*i.e.* transitory decrements in forced expiratory volume in one second (FEV_1) of at least 20%, signifying asthma), than the responses to the respiratory questionnaire.

From this study, it was postulated that using methacholine-induced bronchoconstriction as a physical illustration of an asthmatic reaction and recording subjects' familiarity with the associated sensations might be a useful adjunct in the identification of asthma in epidemiological settings, by aiding the interpretation of symptoms and airway-responsiveness measurements. The results of a further epidemiological study in which these techniques were used are now reported.

Methods

The study was part of an epidemiological investigation of respiratory symptoms and airway responsiveness in the north of England. The methodology and the primary results have been reported previously [18, 19]. In all, 608 males and 314 females, aged 20–44 yrs and randomly identified from respondents to a postal survey were studied. All participants gave written informed consent and the study was approved by the local Ethics Committees.

All subjects answered an interviewer-administered questionnaire derived from that used in the study of shipyard workers and the European Respiratory Health Survey Questionnaire [17, 18]. Questions designed to identify asthma were: 1) Have you ever had a wheezing or whistling sound in your chest? 2) Have you ever had episodes of chest tightness? 3) Have you ever had episodes of undue shortness of breath? 4) Have you ever had asthma? 5) Are you currently taking medication for asthma?

In total, 876 subjects underwent measurements of ventilatory function and airway responsiveness, which was quantified as the provocative dose of methacholine causing a 20% fall in FEV_1 (PD_{20}) using a locally developed dosimeter and protocol [20]. Following measurement of baseline FEV_1, sequential cumulative doubling doses of methacholine were administered (dose range 3.125–6,400 µg) at five minute intervals until a >20% decrement in FEV_1 from baseline was attained, or the maximum dose of 6,400 µg had been administered. The PD_{20} was quantified by linear interpolation from the dose-response plot.

The ability to perceive bronchoconstriction was assessed at the end of the methacholine test, *i.e.* at a time when subjects were maximally bronchoconstricted, by asking: "Compared to before the methacholine test, does your chest now feel any different?" Subjects were asked 1) if they would describe any change in their respiratory sensations as "wheezing", "chest tightness" or "breathlessness", and 2) if they had ever experienced similar sensations previously, and, if so, under what circumstances?

Results were analysed using the STATA Release 3 statistical package (Computing Resource Center, Santa Monica, CA, USA). The majority of subjects with quantifiable levels of airway responsiveness (PD_{20} ð6,400 µg) had similar falls in FEV_1 in the range 20–25% from baseline, whereas those with unquantifiable levels (PD_{20}> 6400 µg) had FEV_1 falls which were of smaller magnitude and distributed over a wider range (0–19.9%). The two groups were, therefore, examined separately. However, because several variables and associations were common to both groups, the results presented here are those of the two combined groups, with any differences highlighted.

Results

Basic anthropometric, clinical and airway responsiveness data are detailed in table 1. The mean±SD age of the 876 subjects was 34±7 yrs and 67% were males. The lifetime prevalence of wheeze reported on the questionnaire was 43%, chest tightness 35% and undue breathlessness 22%. The lifetime prevalence of diagnosed asthma was 12%, and 8% of subjects were currently using asthma medication. Quantifiable levels of airway responsiveness (PD_{20} ð6,400 µg) were measured in 34%, and airway responsiveness in the range considered to be consistent with untreated active asthma (PD_{20} ð1,000 µg) was present in 21% [21]. Symptoms, previous diagnosis of asthma and use of medication were all strongly associated with the level of airway responsiveness, as shown in figure 1.

A total of 818 (93%) subjects were asked if they perceived any difference in their respiratory sensations at the end of the methacholine test and of these, 59% (485) perceived some change. The question was inadvertently omitted for 58 subjects. The probability of perceiving bronchoconstriction was directly related to its magnitude, increasing by 13% for every 5% decrement in FEV_1, as shown in figure 2 and table 2. In subjects with unquantifiable levels of airway responsiveness (PD_{20} >6,400 µg and FEV_1 decrement <20%) this association was highly significant ($p<0.001$). In those subjects with quantifiable levels of airway responsiveness (PD_{20} ð6,400 µg) the association was not significant because of smaller numbers and because all these subjects had a FEV_1 decrement Š20%, a degree of bronchoconstriction which was perceived by almost everyone. Younger subjects and females were more

Table 1. – Age, sex, symptom profile and presence or absence of diagnosed treated asthma for all subjects, and by level of airway responsiveness (as assessed by provocative dose of methacholine causing a 20% fall in forced expiratory volume in one second (PD_{20}))

	PD_{20} ð1000 µg n=183 (20.8)	PD_{20} 1000–64000 µg n=116 (13.2)	PD_{20} >6400 µg n=577 (65.9)	All subjects n=876
Mean age yrs	32.8	33.4	33.8	33.6
(95% CI)	(31.7–33.8)	(32.0–34.8)	(33.3–34.4)	(33.1–34.0)
Males	97 (53.0)	67 (57.8)	423 (73.3)	587 (67.0)
Ever wheezed	140 (76.5)	57 (49.1)	182 (31.7)	379 (43)
Ever had chest tightness	109 (59.6)	50 (43.1)	146 (25.6)	305 (35.1)
Every unduly short of breath	79 (43.2)	37 (31.9)	74 (12.9)	190 (21.7)
At least one symptom	150 (82.0)	75 (64.7)	259 (44.9)	484 (55.3)
Ever had asthma	73 (39.9)	14 (12.1)	20 (3.5)	107 (12.2)
Currently using asthma medication	54 (29.8)	9 (7.8)	5 (0.9)	68 (7.8)

Percentages are shown in parenthesis. CI: confidence interval.

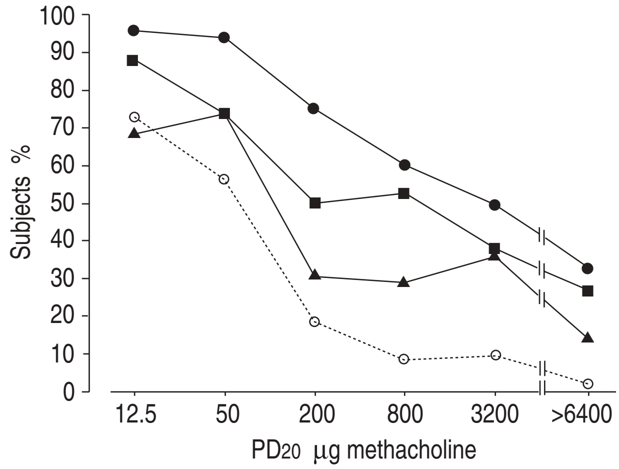

Fig. 1. – Percentage of subjects with symptoms, diagnosed asthma or currently using asthma treatment, by airway responsiveness. ●: ever wheezed; ■: ever had chest tightness; ▲: ever unduly short of breath; ○: current asthma treatment. PD_{20}: provocative dose (of methacholine) causing a 20% fall in forced expiratory volume in one second.

likely to perceive bronchoconstriction. Symptomatic subjects were more likely to perceive bronchoconstriction, but this association was only significant in subjects with unquantifiable levels of airway responsiveness (PD_{20}> 6,400 µg), probably because of the high (75%) overall prevalence of symptoms amongst those with quantifiable levels of airway responsiveness ($PD_{20} \leq$ 6,400 µg), as shown in tables 1 and 2. There were no further independent significant associations with diagnosed asthma, use of medication or baseline ventilatory function.

Of the 485 subjects who were able to perceive bronchoconstriction, 280 (58%) reported that they had experienced a similar sensation in the past. This familiarity with bronchoconstriction was independently associated with the reporting of respiratory symptoms on the questionnaire, a diagnosis of asthma and level of airway responsiveness, as shown in figure 3 and table 3. Familiarity with bronchoconstriction was not associated with the magnitude of induced bronchoconstriction, age, sex or baseline FEV_1 expressed either as an absolute value or as the percentage of the predicted value.

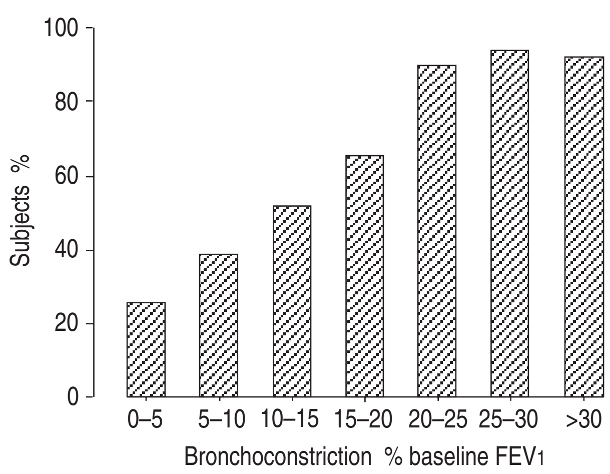

Fig. 2. – Percentage of subjects perceiving bronchoconstriction by percentage reduction in forced expiratory volume in one second (FEV_1).

Table 2. – Logistic regression analysis relating the probability of perceiving bronchoconstriction to the percentage of bronchoconstriction induced, age, sex and number of positive symptoms reported by questionnaire

	Odds ratio	95% CI	p-value
Induced bronchoconstriction % of baseline FEV_1	1.13	1.11–1.16	<0.001
Age yr^{-1}	0.97	0.94–0.99	0.01
Sex (females *vs* males)	1.73	1.18–2.55	0.005
One *vs* no symptoms	1.56	1.03–2.37	0.04
Two *vs* no symptoms	2.84	1.65–4.89	<0.001
Three *vs* no symptoms	3.09	1.65–5.78	<0.001

Symptoms: "Ever wheezed", "ever had chest tightness" and "ever unduly short of breath". CI: confidence interval.

Subjects with a current or previous diagnosis of asthma were more likely to experience a 20% decrease in FEV_1 and to be familiar with the associated sensations than subjects who had never had a diagnosis of asthma: 79% (79/100) *versus* 10% (71/718). There were 110 subjects with quantifiable levels of airway responsiveness ($PD_{20} \leq$6,400 µg) who had never had a diagnosis of asthma, but who had the potential to attract such a diagnosis because they reported familiarity with the sensations of bronchoconstriction. When asked about similar previous episodes, 65 (59%) had experienced the sensations associated with substantial bronchoconstriction in the previous year and 35 (32%) had experienced such sensations on five or more occasions in the previous year.

Amongst those reporting familiarity with bronchoconstriction, the sensations associated with induced bronchoconstriction were described as "wheezing" in 62% of subjects, "chest tightness" in 89% and "breathlessness" in 56%. Two or more symptoms were reported by 72%. Subjects who perceived the sensations but denied previous experience of them used fewer descriptive terms (p<0.001), with 37% describing them as "wheezing", 35% as "breathlessness" and 83% as "chest tightness" and 44% reporting two or more symptoms.

There was surprisingly little agreement between the symptoms reported by the questionnaire and the symptoms used to describe the sensations associated with induced

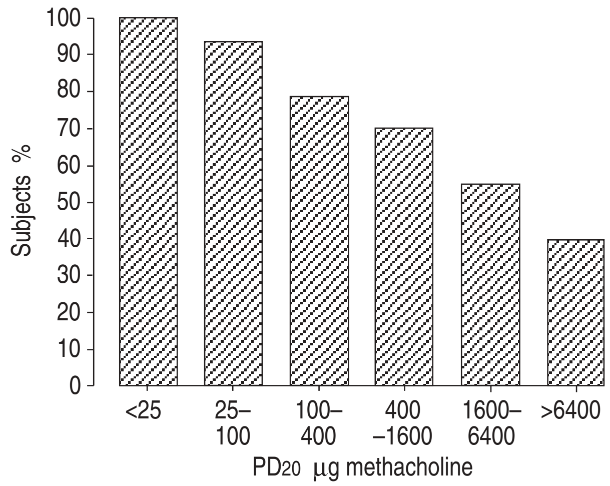

Fig. 3. – Percentage of subjects familiar with the sensations of bronchoconstriction, by airway responsiveness as assessed by provocative dose of methacholine causing a 20% fall in forced expiratory volume in one second (PD_{20}).

Table 3. – Logistic regression analysis relating the probability of subject familiarity with the sensations of bronchoconstriction to questionnaire-reported symptoms, diagnosed asthma and the provocative dose of methacholine causing a 20% fall in forced expiratory volume in one second (PD_{20}), in subjects perceiving bronchoconstriction

	Odds ratio	95% CI	p-value
One *vs* no symptoms	4.61	2.69–7.91	<0.001
Two *vs* no symptoms	16.3	8.28–32.1	<0.001
Three *vs* no symptoms	39.6	12.9–121.4	<0.001
Ever diagnosed asthmatic	7.24	1.55–33.8	0.01
PD_{20} ð6400 *vs* >6400 µg	2.20	1.37–3.54	0.001

Symptoms: "Ever wheezed", "ever had chest tightness" and "ever unduly short of breath". CI: confidence interval.

bronchoconstriction. The Kappa statistic [22] was used to express the relative agreement between the two and the calculated values were 0.23 for wheeze, 0.16 for chest tightness and 0.26 for breathlessness, indicating poor-to-fair agreement. There were three areas of disparity between the questionnaire and bronchoconstriction elicited symptoms, best illustrated by the 261 subjects able to perceive significant (Š20%) bronchoconstriction. For this group, the questionnaire prevalence of current or previous wheezing was 67% (175), but 18 (10%) of these subjects reported no familiarity with the sensations of methacholine-provoked bronchoconstriction, suggesting that they had used the term "wheeze" to describe some other (non-bronchoconstriction) phenomenon. The remaining 157 subjects reported familiarity with bronchoconstriction, and of these, 29% (46) used a term other than wheeze to describe bronchoconstriction, despite having reported wheeze on the questionnaire. A further 18 of the 32 (56%) subjects who denied wheezing on the questionnaire used the term to describe methacholine-induced bronchoconstriction, suggesting a false-negative questionnaire response. In total, there was disagreement between the questionnaire and postbronchoconstrictor reports of wheeze in 31% of subjects with a quantifiable PD_{20}, able to perceive the induced bronchoconstriction. Similar findings were noted for other symptoms and for subjects with <20% bronchoconstriction.

Discussion

In this study methacholine-induced bronchoconstriction was used as a physical illustration of the respiratory sensations associated with asthma, and its relationships with the responses to a respiratory questionnaire and with airway responsiveness determined. Previous studies have shown that the perception of breathlessness is not dependent on the nature of the stimulus provoking immediate bronchoconstriction [23]. It was, therefore, anticipated that reported familiarity with methacholine-provoked symptoms should give some indication of previous experience of significant bronchoconstriction, *i.e.* asthma. Factors which have been previously reported to influence the perception of bronchoconstriction include the magnitude of bronchoconstriction, age, sex, prechallenge breathlessness, diagnosed asthma, airway responsiveness, atopy and smoking [24, 25], although the associations with several of these variables have not been consistently demonstrated.

In the study population, the ability to perceive bronchoconstriction was clearly related to its magnitude, with 71% of subjects experiencing a Š10% decrement in FEV_1 being able to perceive it. This proportion is similar to that found by Brand *et al.* [25] who showed that 76% of their population were aware of a 10% histamine-provoked decrement in FEV_1. Bronchoconstriction beyond 20% did not increase the proportion of subjects recognizing the sensation, suggesting that a small number of subjects have very poor perception. The ability to perceive bronchoconstriction was associated with the reporting of respiratory symptoms on the questionnaire, even amongst individuals with low levels of airway responsiveness, who experienced only small decrements in FEV_1. This highlights the importance of individual variability in the awareness of respiratory sensations as an independent determinant of the recognition and reporting of respiratory illness. It also represents the corollary to the identification by Brand *et al.* [25] of a group of hyperresponsive subjects who were unable to identify bronchoconstriction, and who reported no asthmatic symptoms.

Females were more aware of a given degree of bronchoconstriction than males. Population studies suggest that after adjustment for baseline FEV_1, there is no sex difference in the distribution of airway responsiveness. There is, however, a female predominance in the diagnosis of adult asthma. This has been attributed to diagnostic bias [26], but our data suggest that it might be a manifestation of a greater ability of females to perceive bronchoconstriction. Sex differences in the perception of respiratory sensations might also explain other phenomena such as the female predominance in reporting respiratory side-ef-fects of angiotensin-converting enzyme-inhibitors in the absence of an excess of cardiovascular side-effects [27].

Just over half of those who were able to perceive bronchoconstriction were familiar with the associated sensations. Unlike the ability to perceive bronchoconstriction, the subjects' familiarity with the sensations was independent of the magnitude of the bronchoconstriction induced. It was associated with the presence of respiratory symptoms on the questionnaire, a diagnosis of asthma and the degree of airway responsiveness, and these associations support its validity as a measure of asthma in epidemiological studies. It is clear, however, that a greater proportion of the population are familiar with bronchoconstriction than have clinically apparent "asthma". Physiologically, asthma is quantitatively rather than qualitatively different from normality and so conventionally "nonasthmatic" subjects probably do experience significant degrees of bronchoconstriction from time to time in response to potent environmental stimuli [28]. Awareness of this bronchoconstriction is likely to explain, at least partly, the high prevalence of asthmatic symptoms reported in most epidemiological studies of young adults [4, 18, 29].

At high levels of airway responsiveness, *i.e.* PD_{20} ð200 µg using our techniques, the majority of subjects perceive and recognize their marked bronchoconstriction, report their symptoms and receive a diagnosis of asthma. At intermediate levels of airway responsiveness, *i.e.* within the PD_{20} range 200–1,000 µg, only about 20% of subjects have a diagnosis of asthma. These subjects are no different from those without asthma in terms of airway physiology or their ability to perceive bronchoconstriction, with the majority of both diagnosed asthmatics (95%) and nonasthmatics (70%) reporting familiarity with bronchoconstriction. This suggests that willingness to report symptoms to a physician and willingness on the part of the physician to establish a diagnosis are important determinants of the probability of an individual being diagnosed as asthmatic. Numerical considerations suggest that subjects with intermediate levels of airway responsiveness are a potentially important group. The lifetime prevalence of diagnosed asthma in our study was 12%, but a further 7% had levels of airway responsiveness consistent with asthma and had previous experience of substantial bronchoconstriction, and so had the potential to attract a diagnosis of asthma. If changes in awareness and diagnostic criteria affect these subjects, then there is the potential for the apparent prevalence of asthma to increase by nearly 60%.

The language used to describe asthma is particularly important for epidemiological studies using symptom questionnaires. It is assumed that the responses to questionnaires reflect subjects' experience of bronchoconstriction. This is not necessarily so as the reporting of symptoms depends on psychological profiles [6], the setting in which the study takes place [21], respiratory diseases other than asthma, and probably, other factors. There was discordance between the terminology used to describe bronchoconstriction on the questionnaire and after the inhalation of methacholine in 27% of our study population. Questionnaire responses, therefore, do not necessarily give an accurate picture of the asthmatic sensations experienced by a group of subjects.

This study has demonstrated that recognition of induced bronchoconstriction has all the appropriate associations expected of a measure of asthma prevalence. In studies incorporating measurement of airway responsiveness, the perception of, and familiarity with, induced bronchoconstriction is simple to ascertain. Recording familiarity with bronchoconstriction may aid the interpretation of symptom questionnaires and airway responsiveness measurements and give a closer insight into the true prevalence of bronchoconstriction and asthma.

References

1. Gregg I. Epidemiological aspects. *In*: Clark TJH, Godfrey S, eds. Asthma. 2nd Edn. London, Chapman & Hall, 1983; pp. 242–284.
2. Samet JM. Epidemiologic approaches for the identification of asthma. *Chest* 1987; 91: 74S–78S.
3. Anderson HR, Bland JM, Peckham CS. Risk factors for asthma up to 16 years of age. *Chest* 1987; 91: 127S–130S.
4. Bjornsson E, Plaschke P, Norman E, *et al*. Symptoms related to asthma and chronic bronchitis in three areas of Sweden. *Eur Respir J* 1994; 7: 2146–2153.
5. Sparrow D, O'Connor G, Colton T, Barry CL, Weiss ST. The relationship of nonspecific bronchial responsiveness to the occurrence of respiratory symptoms and decreased levels of pulmonary function. *Am Rev Respir Dis* 1987; 135: 1255–1260.
6. Dales RE, Spitzer WO, Schechter MT, Suissa S. The influence of psychological status on respiratory symptom reporting. *Am Rev Respir Med* 1989; 139: 1459–1463.
7. Dodge RR, Burrows B. The prevalence and incidence of asthma and asthma like symptoms in a general population sample. *Am Rev Respir Dis* 1980; 122: 567–575.
8. Littlejohns P, Ebrahim S, Anderson R. Prevalence and diagnosis of chronic respiratory symptoms in adults. *Br Med J* 1989; 298: 1556–1560.
9. Anthonisen R, Wright EC. Bronchodilator response in chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1986; 133: 814–819.
10. Eliasson O, Degraff AC. The use of criteria for reversibility and obstruction to define patient groups for bronchodilator trials. *Am Rev Respir Dis* 1985; 132: 858–864.
11. Cockcroft DW, Killian DN, Mellon MA, Hargreave FE. Bronchial reactivity to inhaled histamine: a method and clinical survey. *Clinical Allergy* 1987; 7: 235–243.
12. Kelly CA, Ward C, Stenton SC, Bird G, Hendrick DJ, Walters EH. Number and activity of inflammatory cells in bronchoalveolar lavage fluid in asthma and their relation to airway responsiveness. *Thorax* 1988; 43: 684–692.
13. Kelly CA, Stenton SC, Ward C, Bird G, Hendrick DJ, Walters EH. Lymphocyte subsets in bronchoalveolar lavage fluid obtained from stable asthmatics, and their correlations with bronchial responsiveness. *Clin Exp Allergy* 1989; 19: 169–175.
14. Rogers DF, O'Connor BJ. Airway hyperresponsiveness: relation to asthma and inflammation. *Thorax* 1993; 48: 1095–1096.
15. Cockcroft DW, Berscheid BA, Murdock KY. Unimodal distribution of bronchial responsiveness to inhaled histamine in a random human population. *Chest* 1983; 83: 751–754.
16. Rijcken B, Schouten JP. Measuring bronchial responsiveness in epidemiology. *Eur Respir J* 1993; 6: 617–618.
17. Stenton SC, Beach JR, Avery AJ, Hendrick DJ. Asthmatic symptoms, airway responsiveness and recognition of bronchoconstriction. *Respir Med* 1995; 89: 181–185.
18. Devereux G, Ayatollahi T, Ward R, *et al.* Asthma and airway responsiveness to two Health Districts of Northern England. *Thorax* 1996; 51: 169–174.
19. Devereux G, Beach JR, Bromly C, *et al.* Does dietary sodium influence airway responsiveness and is it important in asthma epidemiology? *Thorax* 1995; 50: 941–947.
20. Beach JR, Young CL, Avery AJ, *et al.* Measurement of airway responsiveness to methacholine: relative importance of the precision of drug delivery and method of assessing response. *Thorax* 1993; 48: 239–243.
21. Stenton SC, Beach JR, Avery AJ, Hendrick DJ. The value of questionnaires and spirometry in asthma surveillance programmes in the workplace. *Occup Med* 1993; 43: 203–206.
22. Altman DG. Practical Statistics for Medical Research. London, Chapman & Hall, 1991.
23. Turcotte H, Corbeil F, Boulet L. Perception of breathlessness during bronchoconstriction induced by antigen, exercise, and histamine challenges. *Thorax* 1990; 45: 914–918.
24. Burdon JGW, Juniper EF, Killian KJ, Hargreave FE, Campbell EJM. The perception of breathlessness in asthma. *Am Rev Respir Med* 1982; 126: 825–828.
25. Brand PLP, Rijcken B, Schouten JP, Koeter GH, Weiss ST, Postma DS. Perception of airway obstruction in a random population sample. *Am Rev Respir Med* 1992; 146: 396–401.
26. Dodge RR, Burrows B. The prevalence and incidence of asthma and asthma like symptoms in a general population sample. *Am Rev Respir Dis* 1980; 122: 567–575.
27. Moore N, Noblet C, Joannides R, Ollagnier M, Imbs JL, Lagier G. Cough and ACE inhibitors. *Lancet* 1993; 341: 61.
28. Josephs LK, Gregg I, Mullee MA, Holgate ST. Nonspecific bronchial reactivity and its relationship to the clinical expression of asthma. *Am Rev Respir Dis* 1989; 140: 350–357.
29. Jarvis D, Lai E, Luczynska C, Chinn S, Burney P. Prevalence of asthma and asthma like symptoms in young adults living in three East Anglian towns. *Br J Gen Pract* 1994; 44: 493–497.