Do Respiratory Symptoms Predict Chronic Airflow Obstruction and Bronchial Hyperresponsiveness in Older Adults?

Deborah S. Renwick and Martin J. Connolly

University Department of Medicine for the Elderly, Barnes Hospital, Manchester, UK.

RESPIRATORY symptoms are common in adult populations of all ages (1–4). Population studies have shown that symptomatic subjects have a higher prevalence of both obstructive spirometry results (5,6) and bronchial hyperresponsiveness (7,8) than asymptomatic subjects.

Chronic airflow obstruction (CAO) is usually defined in terms of reduced ratio of one second forced expiratory volume to forced vital capacity (FEV1/FVC ratio). It may be associated with either chronic asthma or chronic bronchitis. Although some patients with CAO report cough and sputum production, up to 50% are asymptomatic (5,9). Bronchial hyperresponsiveness (BHR) reflects increased airways lability and is associated with symptomatic asthma (10). In population surveys it is more strongly related to “asthmatic” symptoms (wheeze, breathlessness) than to cough or sputum production (8,9). Despite this, the prevalence of asymptomatic bronchial hyperresponsiveness has been found to be up to 50% in studies of children and young adults (7,11).

Thus, published population studies have failed to find a strong relationship between respiratory symptoms and either CAO or BHR. However, few such studies have contained large numbers of older adults. The high prevalence of respiratory symptoms, and the apparent reluctance of physicians to perform spirometry in this age group (12), means that the relationship between symptoms and respiratory pathology is particularly important in older adults. We measured airways caliber, bronchial responsiveness, and respiratory symptom prevalence in an age-stratified random sample of white adults aged 45–86 years, in order to assess whether symptoms predict CAO and BHR in middle-aged and older adults.

METHODS

The study was approved by the Central Manchester Health Authority Ethical Committee. An age-stratified random sample of adults aged 45 years and older was selected from the practice lists of local family doctors (general practitioners; GPs) using random number tables. GPs then identified those meeting exclusion criteria (non-Caucasian, housebound, confused, or other major illness preventing participation, such as psychiatric disorder, malignant disease). Non-Caucasians were excluded because of interracial differences in bronchial responsiveness (13). During the last 12 months of recruitment, an increase in the number of older adults included was achieved by discarding alternate selected people aged under 70 years.

Eligible subjects were sent a short explanatory letter and a questionnaire concerning diagnosed asthma or chronic bronchitis, respiratory symptoms, smoking habits, ischemic heart disease, and current medications. Respiratory symptoms questions were adapted from the Medical Research Council questionnaire (14), (see Table 1). Returned questionnaires were screened to identify those suitable for methacholine challenge (exclusion criteria: ischemic heart disease, current use of oral steroids, anticholinergic drugs, oral or topical beta-blockers).

Suitable subjects were requested to refrain from caffeine-containing drinks for 12 hours before attendance. Those taking bronchodilators were requested to omit these for 12 hours (in-
haled preparations), 24 hours (oral medications), or 48 hours (sustained release preparations). Attendance was delayed for 6 weeks after any episode of respiratory tract infection or exacerbation of wheezing.

Nonresponders were sent a reminder letter and second copy of the questionnaire after 4 to 6 weeks. A second reminder was sent one month later, with an abbreviated questionnaire omitting respiratory symptoms questions. A random sample of persistent nonresponders thought still to be living locally was contacted by telephone or home visit, and asked to complete the abbreviated questionnaire.

Subjects gave informed signed consent. A 12-lead ECG was performed, and those with evidence of ischemia were excluded from the methacholine challenge. A short interview-administered supplementary questionnaire was completed, including questions about symptoms of bronchial irritability. Baseline spirometry was measured by portable spirometer (Compact, Vitalograph, Buckinghamshire, UK) (mean of 6 recordings reproducible within 10%). Subjects with baseline FEV₁ < 60% predicted (15), or unable to perform reproducible spirometry, were excluded from bronchial challenge.

Methacholine challenge was performed by the Newcastle Dosimeter method (16,17). Briefly, doubling doses of nebulized methacholine were inhaled at 5-minute intervals by the subject, seated and wearing a noseclip. FEV₁ (mean of 3 recordings reproducible within 10%) was measured before each subsequent dose. Endpoints were a 20% decrease in FEV₁, or administration of a maximum cumulative dose of 6.4 mg methacholine. Subjects with 20% fall in FEV₁ were given 1 mg inhaled terbutaline (Bricanyl, Astra Pharmaceuticals, Herts, UK) via a metered dose inhaler and plastic spacer device (Nebuhaler, Astra Pharmaceuticals, Hertz, UK), and remained within the department until FEV₁ had returned to within 90% of prechallenge level.

Data analysis.—The result of methacholine challenge was expressed as methacholine dose required to produce 20% fall from baseline FEV₁ (PD₂₀). Increased nonspecific bronchial responsiveness was defined as PD₂₀ < 100 μg methacholine (18,19). (Conversion to values of PC₂₀ [methacholine concentration producing 20% fall in FEV₁] can be performed using the relationship PD₂₀ < 100 μg is equivalent to PC₂₀ = 1 mg/ml.) Chronic airflow obstruction was defined as FEV₁/FVC ≤ 65% for subjects aged under 65 years; for those aged 65 and older, a predicted value and obstruction was defined as FEV₁/FVC < 70% (20). Using this method, lower limits of normal FEV₁/FVC decline with increasing patient age (older than age 65) and range from 64–56%.

Smoking history was expressed as packyears smoked, where 1 packyear = 20 cigarettes daily for 1 year.

Subgroups were compared by grouped t test and chi-square tables. Statistical analysis was performed using the program Ecstatic (SomeWare, Vermont). In all cases significance was defined at the .05 level.

RESULTS

Of 783 eligible subjects contacted by mail, 723 returned a questionnaire (response rate 92.3%). Respondents were representative of the local population in terms of age and sex distribution; 508 (64.9% of eligible population) completed the full questionnaire, and 215 the abbreviated questionnaire. Sufficient information to determine eligibility for methacholine challenge was available for those completing the full questionnaire. Because of ischemic heart disease or interacting medications, 113 subjects were excluded. The remaining 395 were invited to attend, and 247 did so (62.5% of those invited; 31.5% of total study population). Attendees were slightly younger than the remaining study population (attendees 64.5 years, study population 66.1 years, p < .02), but were representative in terms of sex distribution, reported asthma and bronchitis, respiratory symptoms, and smoking habits (Table 2). The age distribution of attendees is shown in Figure 1.

Of the 247 attendees, 217 attempted methacholine challenge; one could not perform reproducible spirometry, one declined bronchial challenge, 2 had ECG abnormalities, and 26 had baseline FEV₁ < 60% predicted. Nine subjects failed to complete the challenge because of fatigue, cough, or inability to perform reproducible spirometry; satisfactory results were thus available for 208.

Respiratory symptoms were reported by 273 (53.8%) of the 508 subjects returning the full questionnaire (see Table 2). Eighty-six subjects reported only one symptom, 74 two symptoms, 71 three symptoms, and 33 subjects reported all four respiratory symptoms. Of the 247 attendees, 116 (47.0%) reported one or more symptoms of “bronchial irritability” (breathlessness or wheeze on exposure to inhaled irritants/morning wheeze or chest tightness for at least 1 hour/nocturnal breathlessness), and 51 (20.7%) reported chronic cough and sputum production compatible with a diagnosis of chronic bronchitis.

Reporting of respiratory symptoms was strongly associated with smoking. Current smokers reported more wheeze, cough,

| Table 1. Prevalence of Respiratory Symptoms in 508 Questionnaire Respondents |
|-----------------------------|------------------|
| **Symptom** | **% Positive Response** |
| Wheeze* | 35.9 |
| Cough† | 32.3 |
| Sputum‡ | 33.6 |
| Breathlessness§ | 17.4 |

*Does your chest ever sound wheezy or whistling when you breathe?  
†Do you have a cough?  
‡Do you cough up phlem (flem or spit) from your chest?  
§Do you get breathless when walking on the level/walking in the house/sitting at rest?

REPORTING OF RESPIRATORY SYMPTOMS AND AIRWAYS DISEASE

Table 2. Comparison of Attendees and Nonattendees for Bronchial Challenge

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Attendees (n = 247)</th>
<th>Nonattendees (n = 476)</th>
<th>Study Population (n = 783)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>64.5</td>
<td>67.8</td>
<td>66.1</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Women (%)</td>
<td>56.3</td>
<td>57.0</td>
<td>57.2</td>
<td>&gt; .01</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>33.6</td>
<td>30.7</td>
<td>29.2</td>
<td>&gt; .01</td>
</tr>
<tr>
<td>Ex-smoker (%)</td>
<td>38.5</td>
<td>36.8</td>
<td>37.3</td>
<td>&gt; .07</td>
</tr>
<tr>
<td>Asthma (%)</td>
<td>8.5</td>
<td>6.7</td>
<td>7.3</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Bronchitis (%)</td>
<td>16.7</td>
<td>14.7</td>
<td>16.4</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Symptoms (%)‡</td>
<td>57.1</td>
<td>50.8</td>
<td>53.8</td>
<td>.2</td>
</tr>
</tbody>
</table>

*Attendees versus nonattendees or study population.  
†Available for questionnaire respondents (n = 723).  
‡Available for subjects completing full questionnaire (n = 508).
and sputum production than ex- or never-smokers (wheeze: current smokers 50.4%, ex/never-smokers 30.2%, \( \chi^2 = 17.4, p < .0001 \); cough: current smokers 50.0%, ex/never-smokers 25.6%, \( \chi^2 = 26.5, p < .0001 \), sputum: current smokers 50.0%, ex/never-smokers 27.5%, \( \chi^2 = 22.2, p < .0001 \)). Breathlessness and symptoms of bronchial irritability were reported equally by smokers and ex/never-smokers.

Sixty-five attendees (26.4%) had chronic airflow obstruction. These subjects had a higher prevalence of one or more respiratory symptoms (76.6%) than those without airflow obstruction (50% symptomatic; \( \chi^2 = 13.5, p < .001 \)). However, of all subjects reporting chronic cough and sputum production, less than half (47.1%) had spirometric evidence of airflow obstruction. The validity of reported symptoms for the identification of CAO was assessed by calculation of the positive predictive value (PPV; the proportion of symptomatic subjects with proven airflow obstruction), sensitivity (the proportion of those with airflow obstruction who report symptoms), and specificity (the proportion of those without airflow obstruction who are asymptomatic). These results are summarized in Table 3.

The relationship between symptoms and airflow obstruction was also examined in subjects who were not current smokers, and in those with no history of asthma or bronchitis. Of 168 ex- and never-smokers, 35 (20.8%) had CAO, of whom 41.4% were symptomatic. The positive predictive value of one or more symptoms for airflow obstruction in ex- and never smokers was similar to that for the whole subject group (PPV 32.1%, sensitivity 74.3%, specificity 58.7%). Of 161 subjects with no reported history of obstructive airways disease, 28 (17.4%) had CAO, of whom 60.7% were symptomatic. The positive predictive value of one or more symptoms for airflow obstruction in subjects not reporting asthma or bronchitis was lower than that for the whole subject group (PPV 23.9%, sensitivity 60.7%, specificity 59.4%).

Fifty-four attendees (26.0%) had bronchial hyperresponsiveness. BHR was more common in symptomatic than asymptomatic subjects: 36.8% of symptomatic subjects had BHR, compared with 14.6% of asymptomatic subjects (\( \chi^2 = 26.9, p < .0001 \)). However, over one quarter (26.4%) of those with BHR (PD\(_{20} \leq 100\mu g\)) were asymptomatic. Asymptomatic BHR was equally common in adults aged under 65 and 65 years and older.

The symptoms most prevalent in subjects with BHR were wheeze and symptoms of "bronchial irritability" (morning wheeze or chest tightness, nocturnal dyspnea, and wheeze or breathlessness triggered by inhaled irritants). However, symptoms were also common in subjects with normal levels of bronchial responsiveness. The PPV of these symptoms for BHR was low (Table 4).

Thirty-five (23.3%) ex- and never-smokers had BHR, of whom over one third (34.3%) reported no respiratory symptoms. The PPV of symptoms for BHR in these subjects was similar to that for the whole subject group (for wheeze: PPV 51.3%, sensitivity 57.5%, specificity 83.8%). The prevalence of BHR in subjects with no history of asthma or bronchitis was 18.4%, of whom 37.0% were asymptomatic. The PPV of symptoms for BHR in subjects not reporting asthma or bronchitis was lower than that for the whole subject group (for wheeze: PPV 37.8%, sensitivity 51.8%, specificity 81.3%).

DISCUSSION

The high response rate to the postal questionnaire makes it likely that our study population was representative of local white inhabitants; the proportion of women was similar to estimates for this area (21). Despite the small numbers of subjects attending for
bronchial challenge, this group was representative of questionnaire respondents in terms of smoking habit, respiratory symptoms, and diagnosed asthma and chronic bronchitis. Problems in the recruitment of subjects for surveys of bronchial responsiveness, with attendance rates of <50%, have been noted in other studies (1,8).

We have identified high prevalences of respiratory symptoms, CAO, and BHR in this population. Similarly high prevalences of symptoms have been found in other epidemiological surveys (3,4,11). However, the prevalence of CAO, and particularly BHR, appears higher in Central Manchester than elsewhere (5,8). We can only speculate on the reasons for this, which may include the frequency of smoking, high pollution levels, and occupational exposure in this inner-city environment. Because bronchial responsiveness is strongly related to baseline airways caliber, the high prevalence of BHR may partly reflect the large numbers of subjects with CAO in this study.

Although symptoms were more common in subjects with BHR and CAO, approximately one quarter of those with CAO and BHR were asymptomatic. High prevalences of asymptomatic BHR (>50%) have been reported in younger populations (7,11); it may represent asymptomatic, preclinical, or quiescent asthma, or it may be the temporary result of viral infection or exposure to an inhaled allergen or irritant. The latter is unlikely in our subjects, as viral infection and acute wheezing led to the postponement of bronchial challenge. High prevalences of asymptomatic CAO have also been reported (5,9), and may represent the insidious development of airflow obstruction, or denial of symptoms by smokers.

In a population study of younger adults (mean age 48 years), Mortagy et al. (1) identified a group of symptoms of "bronchial irritability" (breathlessness or wheeze on exposure to respiratory irritants, breathlessness at night, and morning wheeze/chest tightness for at least one hour) that were strongly associated with diagnosed asthma and BHR. The presence of one or more of these symptoms plus BHR was termed the "bronchial irritability syndrome." Two subsequent studies have failed to confirm the existence of this syndrome in adults age 65 and older (4,22); similarly, we have failed to show a strong association between bronchial irritability symptoms and BHR in adults over 45 years. It is possible that the results reported by Mortagy et al. were the result of a particularly strong association between bronchial irritability symptoms and BHR in only the youngest members of their study population.

The relationships between CAO and symptoms, and between BHR and symptoms, were not affected by age in our population. The low PPV of symptoms for both CAO and BHR means that respiratory symptoms do not reliably predict the presence of airflow obstruction or BHR in older adults. The differential diagnosis of respiratory symptoms in this population is wide and includes nonrespiratory diagnoses such as ischemic heart disease, post-nasal drip, and gastro-esophageal reflux. Further investigation including spirometry, measurement of bronchodilator reversibility, and monitoring of peak flow recordings is necessary to identify patients who may benefit from treatment with bronchodilators and/or steroids.

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Address correspondence to Dr. D. S. Renwick, Senior Registrar, Department of Medicine for the Elderly, Camborne/Redruth Community Hospital, Barncoose Terrace, Redruth, TR15 3ER, Great Britain.

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