Natural History of Asthma*

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Although the natural history of asthma has been the subject of several studies,1-6 several questions remain concerning factors that relate to the occurrence of relapses and remissions. This report examines these factors in a community population sample derived from the Tucson Epidemiologic Study of Obstructive Airways Disease. The overall objective is to examine the development of airways disease within the Tucson community.

METHODS

The study population consists of 2,300 subjects followed for a minimum of 8.5 years (mean 9.4 years). At enrollment, subjects completed respiratory questionnaires and underwent physiologic testing. In addition, blood tests including serum IgE and blood eosinophil counts were completed. Cases of active asthma and ex-asthma were defined on the basis of the questionnaire, and 9 or 9 years later, rates of remission and of relapse were determined. The data collected in the first year were then analyzed for factors that were predictive of either a remission or a relapse.

Active asthma was defined as a "yes" response to the question, "Have you ever had asthma?" and at least one of the following: (a) "yes" to the question, "Are you presently taking medication or treatment for your asthma?"; (b) a response of at least "one attack" to the question, "During the past year, how many attacks of asthma have you had?"; or (c) on a scale of 1 (rarely) to 5 (very often), a frequency of at least 3 (frequent) to the question, "If you have had attacks of shortness of breath with wheezing, how often are you bothered by such attacks?" Ex-asthma was identified by a positive response to the question, "Have you ever had asthma?" but a negative response to asthma medications, asthma attacks, or frequent attacks of shortness of breath with wheezing.

Remission and relapse rates were determined by comparison of questionnaire responses in the first and seventh surveys. A remission occurred if a subject fulfilled the criteria for active asthma in the first survey and for ex-asthma in the seventh survey. Similarly, a relapse was defined as ex-asthma in the first survey and active asthma in the seventh survey.

RESULTS

Remission of Asthma

In the first survey, 136 subjects were identified as having active asthma. This represents 6% of the population base. At the end of the survey, 39 of these 136 subjects with active asthma were in remission—a 28.7% remission rate. The remission rate was highest in the 10 to 19-year age group, with 13 of 20, or 65%, having a remission, and lowest in the 40 to 49-year-old subjects, with 1 of 17, or 6%, remitting. Overall, there was a high remission rate in adolescence, a low rate of remission in middle age, and an increase in the rate after age 60.

When the data collected in the first year were analyzed, the presence of the following factors were found to decrease significantly the chance of a remission: wheeze on most days; frequent asthma attacks defined as greater than 12/year; frequent attacks of shortness of breath with wheezing, chronic productive cough; abnormal FEV1; and a coexisting diagnosis of chronic bronchitis or emphysema.

Of all variables analyzed, frequent attacks of shortness of breath with wheeze had the most adverse affect on the probability of remission. Only 1 of 36 (2.8%) subjects with frequent attacks in the first questionnaire subsequently had a remission, while 37 of 98 (37.8%) with less than frequent attacks had a remission (p<.001).

A normal initial FEV1 was the physiologic variable that most favorably affected the remission rate, with 25 of 39 (42.4%) subjects with a normal initial FEV1 having a remission. Only 6 of 39 (15.4%) subjects with an abnormal initial FEV1 had a remission (p<.01).

Other factors appeared to relate to remission but were not statistically significant. Blood eosinophil counts tended to be lower in those over age 35 who remitted. Skin test reactivity was greater in subjects who remitted if they were over age 55 (p<.05), but an opposite trend that was not statistically significant was noted in younger subjects.

Relapse of Asthma

Ninety-nine subjects were considered to be ex-asthmatic in the first survey. Of these, 38 had a relapse, meaning that between the first and last survey they started taking asthma medication or developed active asthma symptoms.

Relapses became more frequent with increasing age. The relapse rate was 27.3% (3 of 11) in subjects aged 10–19 and increased to 67% (8 of 12) in subjects aged 60–69.

We determined which factors related to a relapse of asthma. In the ex-asthmatic patients younger than age 55 who answered "yes" to having any wheeze in the first survey, 23 of 43 (53.5%) became actively asthmatic. If they totally denied wheeze, only 2 of 29 (6.9%) had a relapse (p<.001).

In subjects aged 15–54, 6 of 7 (85.7%) with chronic productive cough had a relapse, whereas 15 of 54 (27.8%) without chronic productive cough had a relapse (p<.01). If attacks of shortness of breath with wheezing were present but infrequent, 11 of 32 (34.4%) relapsed. If such attacks were totally absent, only 6 of 58 (10.3%) relapsed (p<.02).

A subject with an abnormal FEV1 was not significantly more likely to relapse than one with a normal FEV1, although there was a trend in that direction. Blood eosinophil counts did not correlate with relapse. Serum IgE, symptoms of rhinitis, and gender were unrelated either to relapse or to remission of asthma.

Smoking appeared to have an adverse effect on asthma. Current smokers had the lowest remission and the highest relapse rate, while never-smokers had the highest remission and lowest relapse rate. This trend did not reach statistical significance.

CONCLUSIONS

The severity of asthma symptoms as judged by responses to the questionnaire correlated highly with persistence of the disease. The strength of this correlation is striking as illustrated by the symptom of frequent attacks of shortness of breath with wheezing. If this symptom was present, a subsequent remission virtually never occurred. A normal FEV1, presumably indicating less severe disease, favorably influenced the prognosis. Almost half of those with active asthma...
and a normal initial FEV₁ subsequently met the criteria of a remission. Adults considered to have ex asthma frequently relapse unless they are totally free of respiratory symptoms. Adults have a greater chance of both persistence and recurrence of asthma than do children and adolescents.

REFERENCES

Allergy and Nonallergic Bronchial Reactivity As Determinants of Work-related Respiratory Symptoms in Seasonal Grain Handlers

Gerard Ryan, M.D.; W. O. Cookson, M.D.; and A. W. Musk, M.D.

We studied a group of subjects with little or no previous grain dust exposure before and after a short period of grain handling work. The aim of the study was to document work-related symptoms and to determine if there was an association between these symptoms and preemployment respiratory symptoms, allergy skin test responses, and nonallergic bronchial reactivity.

We interviewed 130 consecutive employees before they started work as casual laborers at grain storage sites. There were 110 males and 20 females; the mean age was 20.4 years (range 15-30 years). They answered a questionnaire, had allergy prick skin tests, and measurement of FEV₁ and whole grain (wheat, rye, oats, barley). Nonallergic subjects, and to a fungal extract in 28%. Only 8%.

Symptoms in Seasonal Grain Handling Work. The aim of the study was to document respiratory symptoms, association between these symptoms and preemployment skin test responses, and level of bronchial reactivity. Skin tests were done with Aspergillus, Alternaria, Penicillium, Cladosporium), and whole grain (wheat, rye, oats, barley). Nonallergic bronchial reactivity was quantitated by determining the cumulative dose (pmoles) of inhaled methacholine required to cause a 20% fall in FEV₁, from control level (PD₉₀).

The prevalence of "yes" answers to questions on past symptoms was: cough 10%, wheeze 24%, and breathlessness 8%. Asthma and bronchitis had each occurred in 9%, and 24% had a history of rhinitis. There was a positive skin test to at least one allergen in 54%, to a grain dust extract in 16%, and to a fungal extract in 28%. Only 5 had an FEV₁, <90%

Table 1—Association Between PD₉₀ and Symptoms at Work in Atopic Subjects

<table>
<thead>
<tr>
<th>PD₉₀ (µmol)</th>
<th>Cough</th>
<th>Wheeze</th>
<th>Dyspnea</th>
<th>Rhinitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤4</td>
<td>10</td>
<td>5</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>&gt;4 ≤15</td>
<td>11</td>
<td>3</td>
<td>7</td>
<td>5</td>
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<td>&gt;15 ≤45</td>
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<td>8</td>
</tr>
<tr>
<td>&gt;45</td>
<td>25</td>
<td>2</td>
<td>1</td>
<td>10</td>
</tr>
</tbody>
</table>
| Total      | 60    | 14     | 14      | 13      | 28

*p*Chi-square analysis predicted. The distribution of PD₉₀ was: ≤4 µmole 10%, >4 ≤15 µmole 13%, >15 ≤45 µmole 23%, and 54% had a fall in FEV₁ of less than 20% after the highest dose, 45 µmol. There were no significant differences in any measurements before work between the 19% who smoked cigarettes and those who did not, or between the 33% who had previous grain dust exposure and those who had not.

After the work season, 108 subjects were contacted and asked if work at the grain storage sites had caused cough, wheeze, breathlessness, sneezing, or itchy, runny nose. Three did not work. The mean length of work was 6.5 weeks. Frequency of work-related symptoms was cough 28%, wheeze 13%, and breathlessness 14%; all three symptoms occurred in 10 subjects, 3 of whom left work because of this, and 6 others used some treatment. Symptoms of rhinitis occurred in 35%.

In atopic subjects (≥1 positive skin test response) a lower PD₉₀ (greater airway reactivity) before work was associated with a higher frequency of cough, wheeze and dyspnea (Table 1).

Multivariate regression analysis was used to determine which variables before work were important determinants of symptoms at work. This showed a history of wheeze for work-related cough (coefficient of determination, r² = 0.11); history of wheeze and dyspnea, positive skin test to fungi, PD₉₀ ≤15 for work-related wheeze (r² = .34); and history of dyspnea, positive skin tests to fungi and grain, PD₉₀ ≤15 for work-related dyspnea (r² = .32).

The predictive values of results before work for work-related symptoms were calculated using 2 × 2 tables. Of the subjects who had a history of wheeze and one positive skin test response and PD₉₀ ≤15 together 44% had cough, 65% had wheeze, 56% had breathlessness, and 50% had all three symptoms at work. Fewer than 10% of subjects without these features had work-related symptoms.

The results suggest that preemployment atopy and increased bronchial reactivity are associated with an increased frequency of respiratory symptoms on exposure to grain dust. Second, preemployment history, allergy skin test response, and level of bronchial reactivity may be useful predictors of work-related symptoms. This supports the possibility that symptoms, particularly wheeze and dyspnea, that begin soon after starting work may represent allergen-induced asthma. The weaker association with cough suggests that it may reflect a different mechanism.

REFERENCES