

Nonspecific bronchial hyperresponsiveness and development of asthma in children with hay fever

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It has been suggested that patients with allergic rhinitis who present nonspecific bronchial hyperresponsiveness (BHR) are those most likely to develop asthma. Therefore, a study was conducted in children with rhinoconjunctivitis to ascertain whether BHR to methacholine might predict the development of asthma in these patients. Fifteen patients with hay fever and no previous symptoms of asthma were selected. All underwent clinical symptom tests and methacholine tests, during the pollen season in the 4 consecutive years following the start of the study. At the end of this period, 5 patients had developed asthma. It may thus be affirmed that, in this group, neither the presence nor the degree of previous BHR was useful for predicting which patients would later develop asthma.

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Allergic rhinitis is the most common form of atopic disease, with a prevalence ranging from 5 to 22% (1). Rackemann & Edwards (2), in a 20-year follow-up study of atopic children, found that 20% of patients with allergic rhinitis later developed asthma.

Bronchial hyperreactivity (BHR) is a general finding in asthma (3) and is common in patients with allergic rhinitis (3–5). It has been suggested that patients with allergic rhinitis and BHR are those most likely to develop asthma (3–5).

We studied a group of patients with hay fever to ascertain whether BHR to methacholine could predict development of asthma or whether this depends on other factors such as family history of atopy, total serum IgE levels, duration of hay fever, or seasonal pollen counts.

Material and methods

Patients

Children with seasonal rhinoconjunctivitis who attended our department for the first time in the winter of 1988 (outside the pollen season) were selected. Inclusion criteria were as follows: symptoms of typical hay fever; no previous asthmatic symptoms (chest tightness, wheezing, dyspnea, and chronic coughing not only during the season, but also during respira-

tory infections or exercise); positive prick-test, RAST, and conjunctival provocation to olive and/or grass pollens; no sensitization to perennial allergens; no previous treatment with specific immunotherapy; normal basal spirometry (FVC, FEV₁, and maximum midexpiratory flow >80% of predicted value); and negative methacholine test on the initial evaluation at the start of the study (pollen-free season, winter 1988). All patients were given symptomatic treatment with antihistamines and ophthalmic and nasal disodium cromoglycate during the spring.

Fifteen patients (10 boys, five girls; age range: 6–12 years, mean: 9.6 years) were included in the study. Nine of them had a family history of atopy and five had food allergy. The mean age at the onset of rhinoconjunctival symptoms was 6.6 years (range 2–11 years), and the mean duration of rhinoconjunctivitis at the start of the study was 2.9 years (range 1–9 years). Seven patients were sensitized to olive and grass pollens and eight to grass pollen only. Total serum IgE values varied between 65 and 1125 kU/l, with a mean of 368 kU/l.

Study design

Each patient was reevaluated by one of the authors annually during the pollen season (May–June) over

the following 4 years (1989–92). A diagnosis of asthma was accepted if the subject developed episodic wheezing, dyspnea, and/or cough, together with airway obstruction ($FEV_1 < 80\%$ predicted) and/or a positive bronchodilation test (baseline FEV_1 increased $\geq 15\%$ after inhaled salbutamol). BHR was also studied, annually, during the pollen seasons. Those patients who had BHR in the spring were re-challenged in the next pollen-free season (November–December). In patients who developed asthma during the follow-up period, treatment was modified, and no more tests for BHR were performed.

Finally, the presence or absence of asthma was correlated with family history of atopy; total serum IgE levels; age at onset and duration of hay fever; seasonal pollen counts of olive and grass; and the presence, persistence, and degree of BHR during the follow-up period.

Methacholine challenge

The methacholine test was used for BHR study by the method described by Chatham et al. (6) with small modifications. The aerosol was intermittent and was generated with a Hudson-type nebulizer. The subjects were instructed to take slow, deep breaths from residual volume to near total lung capacity. Phosphate-buffered saline (PBS) was inhaled first, followed by successive doses of methacholine: one breath of 5 mg/ml, four breaths of 5 mg/ml, one breath of 25 mg/ml, two breaths of 25 mg/ml, and, finally, four breaths of 25 mg/ml every 5 min. FEV_1 was measured basally and 3 min after each dose. Inhalations were continued until a 20% fall from baseline FEV_1 was obtained or a total dose of 200 accumulated inhalatory units (AIU; 1 AIU = one breath of 1 mg/ml methacholine dilution) was reached. Then, dose-response curves were constructed to calculate $PD_{20}\text{-}FEV_1$ (the methacholine dose required to achieve a 20% reduction in baseline FEV_1).

Pollen counts

Pollen counts of olive and grass were made with a volumetric spore trap. A Burkard trap (Burkard Manufacturing Co., UK) was used. Sampling was done daily in May and June from 1989 to 1992. Total pollen counts were calculated by the sum of daily averages from each spring. Data were provided by Dr J. Subiza of the General Pardiñas Center of Allergy and Clinical Immunology.

Statistical analysis

Nonparametric statistical tests were used for group comparison (Mann-Whitney U test).

Ethical considerations

The study was approved by the local human ethics committee, and informed consent was obtained from the parents of each child.

Results

At the end of the follow-up period, 13 of the 15 patients had airway hyperresponsiveness, and five had developed asthma.

The subjects with only rhinoconjunctival symptoms during the 4-year follow-up period were similar to the five asthmatic patients with respect to mean age (14.2 and 13.4 years, respectively), sex, age at onset of rhinoconjunctival symptoms (5 years for the asthmatics and 7 years for nonasthmatics), and mean total IgE, (602 kU/l in patients who developed asthma and 280 kU/l in those who did not). At the end of the follow-up period, the mean duration of hay fever was 7 years for asthmatics and nonasthmatics. A positive family history of atopy was present in seven of the 10 nonasthmatic patients with hay fever and in two of the five who developed asthma.

One of the patients developed asthma for the first time in the spring of 1989, one (nonresponder in previous pollen season) in spring 1990, one in spring 1991 (nonresponder in previous pollen seasons), and two (who had perennial BHR in the previous 2 years) during the spring of 1992.

Fig. 1 shows the appearance of BHR in the patients throughout the 4-year follow-up period. Olive and grass pollen counts in the pollen season of the 4-year follow-up and the number of asthmatic or hyperreactive patients are depicted in Fig. 2.

Only two of the 10 nonasthmatic patients presented persistently negative methacholine tests

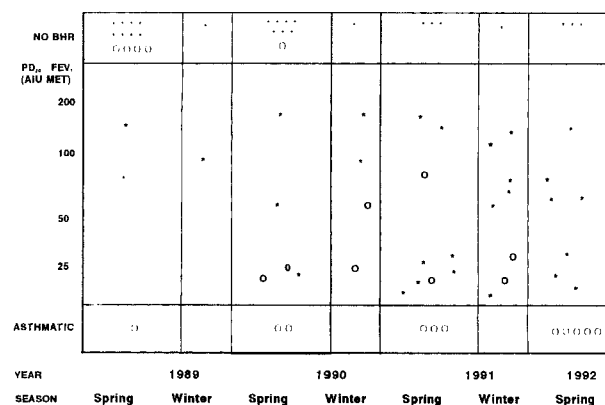


Fig. 1. Nonspecific bronchial hyperresponsiveness and development of asthma in 15 children with hay fever during 4-year follow-up period. Children who developed asthma during study period are indicated by circle ($n = 5$); those who did not, by asterisk ($n = 10$). $PD_{20}\text{-}FEV_1$ (AIU MET) = methacholine dose required to reduce baseline FEV_1 by 20%. S = spring; W = winter.

after 4 years of follow-up. This test was positive at least once in the eight other patients, although results varied in them. For example, one patient presented a positive methacholine test in spring 1990 and negative results thereafter.

Discussion

Allergic rhinitis may be a risk factor for development of asthma. The incidence of asthma in patients with rhinitis differs in the various studies made, and some investigations even fail to confirm this observation. Nevertheless, it is difficult to compare the results because of differences in surveys, methods, age of the patients, etiologic factors, follow-up period, or treatment administered (7–12).

BHR is an almost constant feature of asthma and a common feature in patients with allergic rhinitis. It has been suggested that allergic rhinitis patients who have BHR are those more likely to develop asthma. Because of this, several studies have been performed with contradictory results (4, 7, 14–16).

In our study, despite the small number of patients, we conclude that neither the presence nor the degree of BHR enabled one to predict which patients with allergic rhinitis would develop asthma in the subsequent pollen seasons, since most of our patients with only rhinitis eventually presented seasonal airway hyperresponsiveness, maintained in various cases for several years (even in the pollen-free season) and with PD₂₀ values within the asthmatic range, without presenting symptoms of asthma. On the other hand, some patients who later developed asthma had not shown any BHR in previous springs.

Therefore, it appears that, at least in our patients, other determining factors must be involved in the development of asthma. Smoking (17), immuno-

therapy (18), and degree of antigenic exposure (15, 19) have been proposed as factors which might determine the onset, or not, of asthma and BHR. The first two were ruled out in our group, and we observed that a greater amount of pollen is not associated with a higher number of patients with BHR. It is worth noting that the highest number of patients with BHR and asthma was obtained during the last two springs despite low pollen counts in both seasons. In contrast, in the spring with the highest pollen count (1990), only three of the 10 patients with hay fever presented BHR. It should be emphasized that six of the seven nonasthmatic patients with positive methacholine tests during the fourth pollen season were also hyperresponsive in pollen-free periods.

Although we are unable to draw definite conclusions in view of the small size of our series, our study clearly indicates that most children with hay fever will develop asthma and/or BHR within the following 4 years. Methacholine tests could not be used for the prediction of which children would develop asthma.

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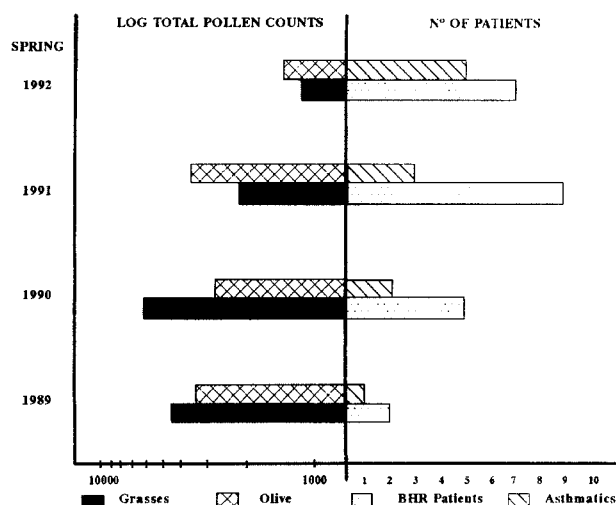


Fig. 2. Total pollen counts of pollen season (spring) in 4-year follow-up period and number of patients with BHR and asthma during each pollen season.

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