

An Epidemiologic Study of Bronchial Asthma and Smoking

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The role of smoking and air pollution in bronchial asthma in otherwise healthy adults is still unclear. We compared 79 cases of asthma, diagnosed between ages 20 and 65 years, with 304 randomly drawn population controls of similar age from the same catchment area as the cases. The comparison involved questionnaire information on smoking habits, occupational exposures, dwelling conditions, various suspect allergenic exposures, and atopy. Those who had smoked for 3 years or more,

present or past, were at increased risk for bronchial asthma (odds ratio = 1.9; 95% confidence interval = 1.1–3.3). Adjustment by multiple logistic regression for age and gender as well as atopy and air pollution at work did not change the relative risk estimate. Exposure to environmental tobacco smoke, or passive smoking, at work involved a slightly greater risk. (Epidemiology 1995;6:503–505)

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The role of tobacco smoking in the development of bronchial asthma (hereafter termed asthma) is controversial. Many clinicians maintain that smoking increases the risk. Several authors have not found any association between asthma and smoking, however,^{1–4} but there are exceptions.⁵ Others have found gender differences, with an increased risk among smoking males, but not among females.^{6,7} The opposite finding, a higher prevalence of asthma among smoking females but little increased risk for smoking males, was reported by Kiviloog *et al.*⁸ The present report focuses on smoking as a possible determinant of asthma in adults, controlling for other factors such as air pollution at work, dwelling conditions, and atopy.

Subjects and Methods

We identified cases of bronchial asthma from two adjacent semirural communities in southeast Sweden. We used questionnaires for exposure assessment. The study base comprised 46,000 inhabitants. The wood industry, especially production of prefabricated wooden houses and furniture, is dominant in the area.

After permission from the National Board of Health and Welfare and the regional ethics committee, and in cooperation with the pharmacies of the two communities, we compiled all prescriptions of beta-agonists, used mainly by persons with asthma, during approximately a 9-month period in 1990. This procedure identified a total of 271 individuals who had received beta-agonist prescriptions. Then we asked the responsible physicians by letter to confirm or refute the asthma diagnosis for each patient who had a prescription. After this first verification of the diagnosis, 182 subjects remained as probably having asthma. The 89 individuals excluded had bronchitis, emphysema, or some other disorder, rather than asthma. We then contacted those who were likely to suffer from bronchial asthma by an introductory letter that preceded a questionnaire. The questionnaire was answered by 167 subjects (92%).

The diagnostic criteria for bronchial asthma that we ultimately applied in the present study were those suggested by the American Thoracic Society,⁹ namely: (a) clinical history of reversible bronchial obstruction; and either (b) pathologic results in metacholine test, that is, at least a 20% decreased forced expiratory volume in 1 second (FEV₁s) after inhalation of metacholine in increasing concentrations from 0.125 to 8 mg per ml; or (c) significant results in reversibility test, that is, inhalation of beta-2-agonists resulting in at least 15% increased FEV₁s. We excluded those persons who did not fulfill these criteria, as determined by the lung specialist. We also excluded those not willing to be examined by the lung specialist. The result was an additional exclusion of 44 subjects. Since we focused on adult asthma, we also excluded cases with onset of disease before age 20 years (another 44 individuals). Thus, 79 persons with

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TABLE 1. Smoking Habits among Cases of Asthma and Controls, with Odds Ratios

Exposure	Number of Exposed		Odds Ratio (95% Confidence Interval)	
	Cases (Total N = 79)	Controls (Total N = 304)	Crude	Adjusted*
Ever-smoking	50	145	1.9 (1.1-3.3)	1.9 (1.1-3.4)
Current smoking	21	100	0.7 (0.4-1.3)	
Ex-smoking	29	45	3.3 (1.8-6.0)	
Passive smoking				
At work	35	104	1.5 (0.8-2.6)	1.5 (0.8-2.5)
At home	26	108	0.9 (0.5-1.5)	

* Adjusted by logistic regression for work place air pollution, occupational animal contact, atopy, age, gender, and, when appropriate, passive smoking at work and ever-smoking.

asthma who were age 20-65 years at diagnosis remained. One of us (JZ) examined all of these cases at the same lung clinic.

As controls, to represent the population of the catchment area for the cases, we randomly selected individuals from the general population register who were 20-65 years old in 1990. The number of controls was 539, or three times as many as the originally identified potential cases. Like the cases, they received an introductory letter followed by the questionnaire a week later. After reminders, 472 (88%) of the controls answered the questionnaire.

The cases were diagnosed in the years 1950-1989. As our interest concerned exposures before the onset of asthma, taken as the year of diagnosis, we had to define an anchor point in time for each control. Therefore, we matched four individuals from the pool of 472 controls to each of the 79 cases by gender, community, and age. This procedure permitted exposure assessment of these controls in relation to the year of diagnosis of the corresponding case. We accepted an average age difference of 4 years between a case and its matched controls within an age range of 0-11 years. Three hundred four controls fulfilled these matching criteria; 12 matched controls were excluded.

ASSESSMENT OF EXPOSURE

The questionnaire for exposure information focused on work place exposures, smoking habits, exposure to environmental tobacco smoke at work and at home, and dwelling conditions. It also included some questions concerning medical issues, including atopy. We classified work place exposures into four different air pollution categories based on how the controls reported air pollution in their respective occupations. We specified smoking habits as ever-smoking, including current smoking and ex-smoking, and considered atopy to occur when a subject had atopic dermatitis or hay fever in childhood, according to information from the questionnaire.

EPIDEMIOLOGIC ANALYSES

We took the year of diagnosis by the responsible physician as the year of onset of asthma. We required a minimum exposure of 3 years for all categories of smok-

ing and other exposures, but there was no lag time requirement regarding time from end of exposure until year of diagnosis, except for ex-smoking. Ex-smoking meant that smoking had ended at least 1 year before onset of asthma. We calculated crude rate ratios for all single exposures that had lasted for 3 years or more and identified confounding by checking for correlation among the controls of the determinants for asthma.¹⁰ We performed the final analyses by using the EGRET package for multiple logistic regression¹¹ and adjusted for age,

gender, air pollution at the work place, occupational contacts with animals, atopy, passive smoking, and ever-smoking.

Results

For the 79 cases, the mean age at diagnosis was 39 years. The mean age of the 304 controls when their matched cases were diagnosed with asthma was 37 years. Of the cases, 57% were males vs 58% of the controls. Three years or more of ever-smoking preceding the year of asthma diagnosis was associated with an almost doubled risk for asthma, with a crude odds ratio (OR) of 1.9, and a 95% confidence interval (CI) of 1.1-3.3 (Table 1). Three years or more of exposure to environmental tobacco smoke at work resulted in a slightly increased risk (OR = 1.5; 95% CI = 0.8-2.6), whereas we found no increased risk for exposure in the home environment (OR = 0.9; 95% CI = 0.5-1.9). Current smoking during the year of diagnosis of asthma was not associated with any increased risk (OR 0.7; 95% CI = 0.4-1.3), whereas ex-smoking was a stronger determinant of risk (OR = 3.3; 95% CI = 1.8-6.0).

Adjustment by multiple logistic regression for atopy, air pollution at the work place in general, occupational contacts with animals, age, and gender did not change the risk estimate for ever-smoking (logistic odds ratio = 1.9; 95% CI = 1.1-3.4). For passive smoking at work places, the OR was 1.5 (95% CI = 0.8-2.5). In the multiple logistic regression analysis, ever-smoked included ex-smoking and current smoking.

Discussion

To ensure the best possible diagnostic validity, and to distinguish asthma from chronic obstructive pulmonary disease, we included in our group a lung specialist (JZ), who applied the diagnostic criteria suggested by the American Thoracic Society.⁹ To our knowledge, these criteria are the best available for practical purposes, and they are superior to criteria often used in previous epidemiologic studies of smoking and asthma. At least six studies have based the diagnosis of asthma on questionnaire reporting of asthmatic symptoms or have accepted the subject's report of a physician's diagnosis of asthma.^{1,2,4-6,12} Five other studies utilized both interview

information and clinical examination for the diagnosis, spirometry included.^{3,7,8,13,14}

To learn whether tobacco smoking is associated with an increased risk of developing asthma, it seems most relevant to evaluate the effect of smoking during a specified time period. In our study, we took this period as 3 years or more preceding the diagnosis; smoking during this period almost doubled the risk for asthma.

Some other authors studying the effects of ever-smoking have not found any increased risk.¹³ The inconsistency may relate to validity; in our study, a physician diagnosed all cases by using reversibility or metacholine tests. Our material included only cases with onset of asthma during adulthood. If we had included persons having asthma during childhood, the background asthma rate would have increased, thereby obscuring the effect of exposures in adult ages. Another strength of our study is that the controls are a random sample of the general population, avoiding selection problems. Furthermore, the response rate to our questionnaire was a high 88% among the controls and 92% among the cases.

Ex-smoking was also associated with a threefold risk. To our knowledge, only two other groups have reported a similar result.^{3,6} The reason for ex-smokers' increased risk might be a tendency for persons with asthma to quit smoking owing to symptoms of asthma.⁶ In contrast, we found current smokers to be at no risk of asthma; this finding is consistent with the complementary view that people without airway problems may continue to smoke.

Our findings for passive smoking varied with the location, home or work. Passive smoking in adults has not been found to be a risk factor for asthma.¹⁵ In contrast, passive smoking is a weak but established risk factor for asthma in children.^{12,16} A meta-analysis of this relation found a risk ratio of 1.2 (95% CI = 1.1-1.4).¹⁶

A mechanism for an increased risk of asthma from smoking is not apparent. It is generally agreed, however, that asthma is a chronic inflammatory process caused by the release of potent mediators.¹⁷ Exposure to agents like chlorine and sulfur dioxide may cause a chronic inflammatory reaction, that is, an irritant-induced asthma.¹³ A persistent asthma syndrome may develop after exposure to high levels of irritants.¹⁴ Cigarette smoke is likely to cause or support a chronic inflammatory reaction, al-

though this possibility is not clearly discussed in the literature in connection with asthma. Also, an increased permeability of the epithelium in the respiratory tract may develop in cigarette smokers.¹⁸ It seems reasonable to speculate that various allergens might more easily reach the submucosal immune-competent cells in smokers¹⁹ and thereby induce an allergic asthma.

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