

Rhinitis as an independent risk factor for adult-onset asthma

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Background: For many years, the association between asthma and rhinitis has primarily been attributed to a common allergic background. Recently, it has been suggested that asthma and rhinitis are associated in the absence of atopy. The nature of this association is not well known.

Objective: The purpose of this study, which was performed in a large, longitudinal community population, was to determine the extent to which rhinitis is an independent risk factor for adult-onset asthma.

Methods: We carried out a nested case-control study from the longitudinal cohort of the Tucson Epidemiologic Study of Obstructive Lung Diseases. One hundred seventy-three incident patients with physician-confirmed asthma were compared with 2177 subjects who reported no asthma or shortness of breath with wheezing. Potential risk factors, including the presence of rhinitis, were assessed before the onset of asthma (patients) or before the last completed survey (control subjects).

Results: Rhinitis was a significant risk factor for asthma (crude odds ratio, 4.13; 95% confidence interval, 2.88-5.92).

After adjustment for years of follow-up, age, sex, atopic status, smoking status, and presence of chronic obstructive pulmonary disease, the magnitude of the association was reduced but still highly significant (adjusted odds ratio, 3.21; 95% confidence interval, 2.19-4.71). After stratification, rhinitis increased the risk of development of asthma by about 3 times both among atopic and nonatopic patients and by more than 5 times among patients in the highest IgE tertile. Patients with rhinitis with persistent and severe nasal symptoms and a personal history of physician-confirmed sinusitis had an additional increased risk of asthma development.

Conclusion: We conclude that rhinitis is a significant risk factor for adult-onset asthma in both atopic and nonatopic subjects. The nature of the association between rhinitis and asthma is open to interpretation. (*J Allergy Clin Immunol* 2002;109:419-25.)

Key words: Asthma, rhinitis, sinusitis, epidemiology, atopy, IgE, skin tests

Epidemiologic studies have consistently reported strong evidence for the association between rhinitis and asthma. Asthma may affect up to 40% of patients with allergic rhinitis, a percentage significantly higher than that in the general population.¹⁻³ Among asthmatic patients, the prevalence rates of rhinitis vary widely according to the age at onset of asthma and can be as high as 80%.^{4,5}

Patients with both lower and upper airway diseases tend to have the onset of rhinitis precede the onset of asthma,^{5,6} although any temporal relationship between the 2 diseases is possible.

Allergic rhinitis is associated with bronchial hyperresponsiveness (BHR), even in the absence of asthma symptoms. Stevens and Vermeire⁷ found histamine responsiveness to be higher among patients with asthma and rhinitis than among patients with rhinitis alone. However, the latter group showed greater bronchial responsiveness than control subjects. BHR among patients with hay fever has been shown to increase during pollen season⁸ and to be predictive of the onset of lower airway symptoms.⁹ However, the sensitivity and specificity of this test in predicting the development of clinical asthma among patients with rhinitis are not known.

Regardless of the presence of BHR, rhinitis has been studied as a potential risk factor for the development of asthma both in children and in adults. Most research on this issue was predicated on the presumption that the association between rhinitis and asthma would be related to a common atopic background.

Among 16,333 children 6 to 7 years old, Rusconi et al¹⁰ found that subjects with persistent wheezing were 10 times more likely to have a positive personal history for allergic rhinitis than control subjects. However, the data were retrospective, and no information was available to determine current atopic status. In a longitudinal study Settipane et al¹¹ found that college freshmen with allergic rhinitis were about 3 times more likely than control subjects to have asthma during a 23-year follow-up period. Similarly, patients aged 18 to 45 years with hay fever have been shown to be at increased risk for asthma in a prospective cohort study in Finland.⁶ In both of the above studies, the relative risks were not adjusted for atopic status.

According to these findings, rhinitis may appear as the first manifestation of a common allergic airway disease,

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Abbreviations used

BHR: Bronchial hyperresponsiveness
 CI: Confidence interval
 COPD: Chronic obstructive pulmonary disease
 OR: Odds ratio

leading eventually to the onset of asthma. Recently, 2 studies have suggested that asthma is associated with rhinitis not only among atopic but also among nonatopic adults.^{12,13}

By investigating cross-sectional data from the European Community Respiratory Health Survey, Leynaert et al¹² found the adjusted odds ratios (ORs) for the association between perennial rhinitis and asthma to be 8.1 among atopic and 11.6 among nonatopic subjects 20 to 44 years old. Similar results were obtained when the analysis was restricted to individuals with normal IgE levels. Similarly, in a longitudinal study Plaschke et al¹³ found that the presence of rhinitis had a strong predictive value for the development of asthma within 3 years among adults with positive, as well as those with negative, skin prick test responses. No information was available about IgE levels.

The role of other potential confounders, effect modifiers, or both in the relationship between rhinitis and asthma is uncertain, particularly in older populations. Among adults, for instance, nasal symptoms have been associated with chronic bronchitis and emphysema, as well as with asthma.¹⁴ This suggests a potential confounding effect of chronic obstructive pulmonary disease (COPD), which has rarely been taken into account.

Although some studies have investigated the relationship between the involvement of sinuses and asthma severity,^{15,16} the presence of a dose-response relationship for the association between rhinitis and asthma has yet to be determined. It is uncertain, for example, whether the severity, duration, or both of nasal symptoms correlate with the risk for asthma.

The purpose of our study was to determine, in a large, longitudinal community population, the extent to which rhinitis is an independent risk factor for adult-onset asthma.

METHODS

We used data that were collected as part of the Tucson Epidemiologic Study of Obstructive Lung Diseases, a prospective cohort study of a stratified cluster sample of 1655 Anglo-white Tucson households enrolled between March 1972 and April 1973. Details of the enrollment process and interview techniques have been previously reported.¹⁷

Between 1972 and 1992, participating subjects were monitored in 12 periodic surveys taken approximately 1.5 to 2 years apart. During each survey, subjects completed a standardized questionnaire and, with the exception of survey 4, performed spirometric lung-function tests.

Allergy skin tests were carried out according to the prick technique up to 3 times for each subject during the study period. The 5 tests used (supplied by Hollister-Stier Laboratories) included some of the most common allergens in the Tucson area: house dust (1:10); Bermuda grass (1:20); tree mix (olive, mulberry, mesquite, and cottonwood;

1:20); weed mix (rabbit bush, saltbush, careless weed, Russian thistle, desert ragweed, and slender ragweed; 1:20); and Dematiaceae mold mix (*Alternaria*, *Helminthosporium*, *Cladosporium*, *Curvularia*, *Spondylocadium*, and *Stemphylium* species; 1:100). A subject was considered atopic if a reaction at least 2 mm greater than the size of the control reaction was recorded for at least one of the 5 tests.

Blood samples were obtained and serum IgE levels were measured up to 3 times for each subject at least 6 years old during the study. The paper radioimmunosorbent test (Pharmacia Diagnostics, Piscataway, NJ) method was used for the measurement of total serum IgE.

Study design and assessment of the risk factors

Within the longitudinal community cohort, we carried out a nested case-control study.

Among subjects who completed at least 2 surveys, we selected 182 subjects who denied past or current presence of asthma at the time of enrollment and had a new physician-confirmed diagnosis of asthma after the age of 20 years during the study period (incident patients). To code their asthma as physician confirmed, we required patients not only to report the presence of asthma but also to have been seen, been given a diagnosis, or been treated for asthma by a physician. We excluded 9 cases for whom any information on the presence of rhinitis in the last 5 years preceding the onset of asthma was missing.

Control subjects were represented by 2177 subjects who reported no asthma or shortness of breath with wheezing at enrollment or during the entire study period. Control subjects were also required to have completed at least 2 surveys, provided information on the presence of rhinitis during the study, and been aged 20 years or older at the last completed survey.

According to the longitudinal nature of our data, we investigated the temporal sequence between exposure to risk factors and the development of asthma. For patients with asthma, the presence of any potential risk factor was assessed at the last nonmissing survey preceding the first report of asthma. Similarly, among the control subjects, potential risk factors were assessed before the last completed survey. Skin test results and IgE levels were assessed at the last measurement preceding the first report of asthma (patients) or the last completed survey (control subjects).

The presence of rhinitis was coded as positive on the basis of an affirmative answer to the following question: "In the last year (or since the last questionnaire), have you had a runny or stuffy nose or episodes of sneezing, apart from colds?"

Rhinitis was defined as persistent if it was present in each of the last 2 surveys before the onset of asthma (or before the last completed survey for control subjects). If it was present only in the last survey before the onset of asthma, it was coded as inconsistent. In 6 of the 12 surveys, patients with rhinitis were asked to rank the severity of their nasal symptoms from 1 to 5: We coded their rhinitis as mild (nasal symptoms ranked 1-2), moderate (3) or severe (4-5). Patients with rhinitis that did not qualify as persistent because they did not complete at least 3 surveys and those who did not rank their nasal symptoms were excluded from the analyses on persistence and severity of rhinitis, respectively.

The presence of sinusitis was assessed as physician-confirmed "sinus trouble" and the presence of COPD was defined as physician-confirmed diagnosis of chronic bronchitis, emphysema, or both at any time before the onset of asthma (patients) or the last completed survey (control subjects).

Statistical methods

Comparisons between normally distributed variables were performed by using parametric tests, including the *t* test for indepen-

TABLE I. Demographic and clinical characteristics of control subjects and asthmatic patients

	Control subjects	Asthmatic patients	P value
No.	2177	173	
Years* of follow-up (mean $\pm$ SD)	11.6 $\pm$ 6.5	9.6 $\pm$ 5.2	<.001
Age† in years (n = 2350; mean $\pm$ SD)	52.96 $\pm$ 21.2	50.81 $\pm$ 19.3	NS
Sex (n = 2350; % male)	47.3	33.5	.001
Positive skin test response (n = 2013; %)	40.1	56.4	<.001
IgE z score (n = 1771; mean $\pm$ SD)	-0.025 $\pm$ 1.0	0.288 $\pm$ 0.9	<.001
Ever smoked (n = 2350; %)	53.7	64.7	<.01
COPD (n = 2350; % ever)	10.2	39.9	<.001
Rhinitis (n = 2350; % positive)	43.8	76.3	<.001
Sinusitis (n = 2329; % ever)	39.8	63.7	<.001

All the risk factors, except age, are reported as they were assessed before the onset of asthma (patients) or before the last completed survey (control subjects). Numbers in parentheses refer to the number of subjects for whom information on the presence of that specific risk factor was available.

*Years included between enrollment and first report of asthma (patients) or between enrollment and last completed survey (control subjects).

†Age at the first report of asthma (patients) or at the last completed survey (control subjects).

Asthma, rhinitis,
other respiratory
diseases

dent samples. According to previously described methods,¹⁸ serum IgE levels of control subjects and asthmatic patients were compared as z scores standardized for sex and age (according to the following age categories: <20, 20-34, 35-49, 50-64, and $\geq$ 65 years). Nonnormally distributed variables were compared by means of the Mann-Whitney test. Comparisons between proportions were performed by using the χ^2 test, and the strength of the association between upper airway diseases and asthma was quantified by means of the OR and tested for statistical significance by using its 95% confidence intervals (95% CI).

The association between rhinitis and asthma was tested for potential confounders, effect modifiers, or both by using logistic regression models and stratification according to the Mantel-Haenszel method. Before including IgE values in logistic regression models, they were log transformed. Missing IgE values were replaced with the mean to avoid dropping subjects from the logistic regression models. Atopic status was treated as a categorical variable (negative [reference], positive, or missing). An α value of .05 for level of significance was chosen for all the statistical tests.

RESULTS

In Table I the demographic and clinical characteristics of control subjects and asthmatic patients are compared. Asthmatic patients had a significantly shorter follow-up period than control subjects (9.6 $\pm$ 5 vs 11.6 $\pm$ 7 years), most likely because in our study we truncated the follow-up at the first report of asthma for patients and followed control subjects until their last completed survey. Subjects with high levels of IgE or positive allergy skin test responses were more likely to have asthma. Female sex, a previous diagnosis of COPD, and a positive history for smoking were other significant risk factors for an asthma diagnosis. More than 76% of the asthmatic patients, a percentage significantly higher than that for control subjects (43.8%), reported the presence of rhinitis before the onset of asthma ($P < .001$). Similarly, almost 64% of asthmatic patients versus less than 40% of control subjects had a previous physician-confirmed diagnosis of sinusitis ($P < .001$).

The possible synergistic effect of rhinitis and sinusitis on the risk of development of asthma is shown in Table II. When compared with subjects without any upper air-

way disease, patients with sinusitis only were not at increased risk for asthma. In contrast, patients with rhinitis only showed a significant OR (2.59; 95% CI, 1.54-4.34) for the association with asthma. This relationship was stronger when both rhinitis and sinusitis were present (OR, 6.28; 95% CI, 4.01-9.82).

As shown in Table III, after adjusting for years of follow-up, age, sex, atopic status, smoking status, and presence of COPD, the association between rhinitis and asthma was still significant. However, the adjusted OR (3.21) was lower than the crude OR (4.13). Because patients with COPD and atopic subjects were more likely to have both rhinitis and asthma, the effect of these 2 confounders accounted for most of the difference between crude and adjusted ORs in our logistic models.

The presence of rhinitis was assessed not only before the first report of asthma but also before the first report of shortness of breath with wheezing (sob-wheezing) in a limited number of patients (Table III). Those were the patients for whom the diagnosis of asthma had been preceded by the onset of respiratory symptoms during the study and for whom information on the presence of rhinitis before the onset of sob-wheezing was available.

Table III shows that the prevalence rates of rhinitis among asthmatic patients were significantly higher than those among control subjects (71.4% vs 43.8%) also when they were assessed before the onset of sob-wheezing. This suggests that rhinitis preceded the onset of lower airway symptoms among patients with undiagnosed asthma.

It should be stated that, despite denying prior asthma, 22.4% of the patients (vs 8.6% of control subjects) recalled "respiratory trouble before age 16" years on the enrollment questionnaire. Among subjects who recalled respiratory trouble in childhood, the OR (6.27; 95% CI, 2.12-18.53) for the association between rhinitis and asthma was particularly high. However, rhinitis had a strong predictive value for the onset of asthma (OR, 3.81; 95% CI, 2.50-5.79) also when the analysis was restricted to the subjects who reported no "respiratory trouble before age 16" years.

TABLE II. ORs for the association with asthma according to the presence of upper airway diseases

	Control subjects	Asthmatic patients	OR	95% CI
Rhinitis –/sinusitis –	847	26	1.00	
Rhinitis +/sinusitis –	453	36	2.59*	1.54-4.34
Rhinitis –/sinusitis +	365	14	1.25	0.64-2.42
Rhinitis +/sinusitis +	493	95	6.28*	4.01-9.82

* $P < .001$.**TABLE III.** ORs for the association with asthma when the presence of rhinitis was assessed before the diagnosis of asthma or before the onset of respiratory symptoms (first report of shortness of breath with wheezing)

	Control subjects, n (%)	Asthmatic patients, n (%)	Crude OR (95% CI)	Adjusted* OR (95% CI)
Rhinitis as assessed before the first report of asthma				
–	1223 (56.2)	41 (23.7)		
+	954 (43.8)	132 (76.3)	4.13† (2.88-5.92)	3.21† (2.19-4.71)
Rhinitis as assessed before the first report of shortness of breath with wheezing				
–	1223 (56.2)	24 (28.6)		
+	954 (43.8)	60 (71.4)	3.20‡ (1.98-5.18)	2.28‡ (1.37-3.78)

*ORs adjusted for years of follow-up, age, sex, atopic status, smoking status, and presence of COPD.

† $P < .001$.‡ $P \leq .005$.**TABLE IV.** Crude and adjusted ORs for the association between rhinitis and asthma after stratification

	Crude OR (95% CI)	Adjusted* OR (95% CI)	Test of homogeneity (P value)
Sex			.112
Male	2.81 (1.60-4.94)	2.11 (1.15-3.88)	
Female	5.10 (3.16-8.24)	4.21 (2.52-7.01)	
Age			.673
20-49 y	3.84 (2.30-6.41)	2.71 (1.57-4.68)	
≥50 y	4.48 (2.70-7.44)	3.85 (2.22-6.67)	
Atopic status			.519
Yes	3.17 (1.81-5.54)	3.02 (1.67-5.45)	
No	4.07 (2.42-6.83)	3.23 (1.85-5.65)	
IgE tertiles			.643
Lowest	3.58 (1.60-8.00)	3.07 (1.31-7.23)	
Intermediate	3.70 (1.97-6.96)	2.94 (1.47-5.86)	
Highest	5.72 (2.55-12.8)	5.78 (2.42-13.8)	
Smoking status			.896
Ever	4.06 (2.59-6.36)	3.04 (1.87-4.93)	
Never	4.27 (2.32-7.86)	3.61 (1.89-6.89)	
COPD			.026
Yes	2.04 (1.12-3.72)	2.54 (1.31-4.94)	
No	4.82 (3.01-7.73)	3.68 (2.25-6.01)	

*ORs are adjusted for years of follow-up and all the other factors included in the Table.

†The test for homogeneity tests the null hypothesis that the crude ORs in the 2 strata are equal.

Table IV shows the crude and adjusted ORs for the association between rhinitis and asthma after stratification by sex, age, atopic status, IgE tertiles, smoking status, and presence of COPD.

The ORs were significant in all the strata. Rhinitis had a significantly lower predictive value for asthma among subjects with a previous diagnosis of COPD than among subjects without COPD. Similarly, the association between rhinitis and asthma appeared stronger among female than among male patients. Although the ORs were

statistically homogeneous in the various categories, rhinitis presented a higher risk for asthma among subjects older than 50 years than among subjects younger than 50 years and among those who never smoked than among smokers. Interestingly, the ORs stratified by atopic status did not differ significantly from each other. After adjustment, subjects with rhinitis were about 3 times more likely to have adult-onset asthma, irrespective of whether they had positive or negative allergy skin test responses. This was not the case for IgE levels. The association between

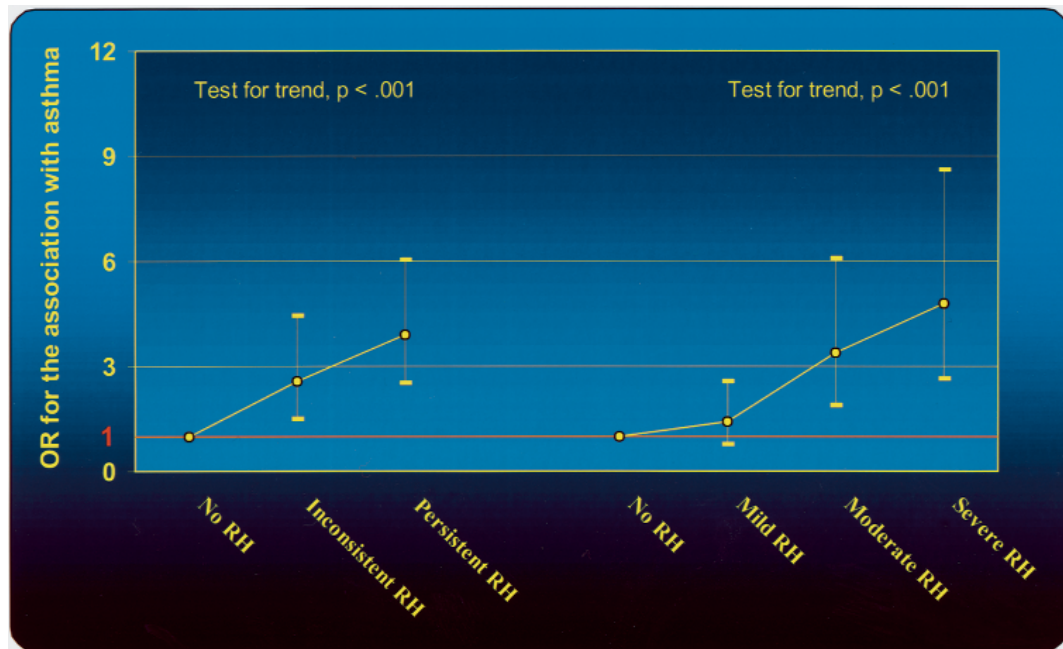


FIG 1. ORs for the association with asthma and 95% CIs across different levels of duration and severity of rhinitis (RH). ORs are adjusted for years of follow-up, age, sex, atopic status, smoking status, and presence of COPD.

rhinitis and asthma appeared stronger among subjects in the highest tertile of IgE z scores than among subjects in the low and intermediate tertiles. Although the result of the test for homogeneity was not significant, this interaction appeared very suggestive.

Because information about the duration of rhinitis and the self-reported severity of nasal symptoms was available, we determined the ORs for the association with asthma across the different levels of exposure (dose-response relationship). Fig 1 shows that as the duration of rhinitis increased, the risk of receiving an asthma diagnosis increased as well. When compared with subjects without rhinitis, patients with self-reported mild nasal symptoms were not at a higher risk for asthma, whereas the ORs for patients with moderate and severe nasal symptoms were significant and increased across the levels.

DISCUSSION

We found rhinitis to be a significant and independent risk factor for adult-onset asthma before, as well as after, the age of 50 years.

The effect of rhinitis on the onset of asthma has been already investigated in longitudinal studies. Huovinen et al⁶ found that hay fever increased the risk of development of asthma during a 15-year follow-up period by 4 times among adult men and by 6 times among women. However, no information on atopic status was available. Similarly, in the cohort of Brown University freshmen,¹¹ both allergic rhinitis and positive skin test responses increased the risk of development of asthma by about 3 times, leading to the question of whether atopic status was acting as a confounder.

The predictive value of rhinitis for asthma, BHR, or both has traditionally been interpreted as the progression of a common airway disease associated with an atopic background. Our findings suggest that rhinitis and asthma are not associated simply because they share atopy as a common risk factor. In agreement with the recent reports from the European Community Respiratory Health Survey,^{12,13} we found rhinitis to be a risk factor for asthma among subjects with negative, as well as positive, skin test responses. In contrast, the association between rhinitis and asthma appeared stronger in the group of subjects with high total IgE levels than in the groups with intermediate and low IgE levels. In our community population the incidence of asthma has been shown previously to correlate with IgE levels more than with skin test reactivity.¹⁸ This suggests that the battery of skin tests could have been inadequate to detect all the important allergens and that IgE levels could be a better indicator for allergy. Particularly, the battery of skin tests that was used in our analyses did not include allergens, such as cat and dog dander, known to be strongly associated with asthma, potentially leading to misclassification of atopic subjects as nonatopic. However, the predictive value of rhinitis for asthma was not restricted only to the group of subjects with high IgE levels. The ORs, although lower, were still significant also among subjects with intermediate and low IgE levels.

Braunstahl et al¹⁹ have shown that segmental bronchial provocation per se can affect the nasal function and mucosa in allergic patients. These findings suggest that an effect of lower airway inflammation on upper airways is possible as well and could facilitate the onset of rhinitis among subjects with respiratory symp-

toms long before having a diagnosis of asthma. Consequently, we assessed the presence of rhinitis among our patients both before an asthma diagnosis and before the first report of shortness of breath with wheezing. In both cases the prevalence rates of rhinitis were significantly higher than those for control subjects. This suggests that our findings were not due to the effect of bronchial inflammation on the upper airway in patients with undiagnosed asthma.

However, the assessment of the temporal sequence between rhinitis and asthma, particularly in an adult population, is complex. Subclinical forms of asthma and some degrees of bronchial inflammation and BHR can be present before the onset of shortness of breath with wheezing. In addition, some adults might not recall having experienced mild asthma symptoms in childhood. Interestingly, despite denying prior asthma, 22.4% of patients with new asthma reported "respiratory trouble before age 16" years. This could represent asthma-like symptoms that began during childhood and were not sufficiently severe to lead to an asthma diagnosis until adult age.²⁰ It should be acknowledged that it is virtually impossible to distinguish with any certainty recrudescence from incident asthma cases in an adult population. In this instance rhinitis might have predicted the relapse rather than the onset of asthma in some of our patients.

The very high prevalence of rhinitis, even among nonatopic subjects, has previously been described in our study population.¹⁸ In the Tucson area a relevant percentage of the nasal symptoms might actually be non-specific reactions to the dry and somewhat dusty environment.¹⁸ However, the presence of nonspecific nasal reactions would be expected to decrease the association between rhinitis and asthma rather than increase it.

In our study less than 40% of the subjects with sinusitis failed to report the simultaneous presence of rhinitis. Among them, the occurrence rates of asthma were not significantly increased when compared with subjects without any upper airway disease. These findings are consistent with those previously published from the Tucson Children's Respiratory Study. In this longitudinal birth cohort physician-diagnosed sinusitis and asthma were no longer associated after controlling for allergic rhinitis and skin test results.²¹ However, it should be stated that in our study positive exposure was assessed differentially for rhinitis and sinusitis. The former was required to be present and active at the last completed survey before the onset of asthma, whereas sinusitis was simply required to have been present at any time before the onset of asthma (lifetime prevalence). The less restrictive temporal relationship could account, at least partly, for the absence of a significant association between sinusitis and asthma.

We also found that rhinitis had a stronger predictive value for asthma when a positive history of sinusitis was present. This finding is consistent with the improvement of asthma symptoms after sinusitis treatment that has been shown in several clinical studies,^{22,23} even in the absence of a direct main effect of sinusitis on asthma.

Bresciani et al¹⁵ found that the clinical symptoms and computed tomography scan scores of rhinosinusitis were significantly greater among patients with severe asthma than among patients with mild-to-moderate asthma. In that study the sinonasal involvement was evaluated among patients already given a diagnosis of asthma. In contrast, in our study any information on the presence and severity of rhinitis was collected before the onset of asthma. We found that both the duration and the severity of nasal symptoms affected the risk of having a diagnosis of asthma, according to a linear dose-response relationship. Such a dose-response relationship should be insensitive to any recall bias.

Several mechanisms have been suggested to explain the influence of nasal dysfunction on the lower airway.^{1,24} First, a neural nasal-bronchial reflex inducing bronchoconstriction or increasing bronchial responsiveness has been invoked. Second, the postnasal drip of inflammatory cells and mediators, their absorption from the nasal mucosa into the systemic circulation, or both have been postulated. Finally, mouth breathing caused by nasal obstruction may reduce filtration, humidification, and warming of inspired air.

There is also convincing experimental evidence that rhinitis treatment can play a direct role in modulating asthma among patients with both diseases. Intranasal use of corticosteroids has been shown to reduce asthma symptoms and bronchial reactivity in patients with both seasonal and perennial respiratory allergy,²⁵⁻²⁷ independently of the deposition of the drug into the lower airway.²⁶ However, to date there has not been conclusive evidence that early treatment of nasal symptoms can modify the progression from rhinitis to asthma. We could not investigate this hypothesis in our study because the information on medication use for nasal symptoms was collected in only a few surveys, and topical nasal therapy was not widely used at the time the study was performed. Specific clinical trials are required to better address this question because they can control for many factors (eg, patients compliance and time and dose of treatment) that are, to a large extent, unknown in epidemiologic studies.

We conclude that rhinitis is a significant and independent risk factor for adult-onset asthma. Our data suggest that rhinitis and asthma are not associated only because they share atopy as a common risk factor. Most likely, the onset of rhinitis, asthma, or both is related to a combination of environmental and genetic factors, some of which peculiarly affect either the upper or the lower airways.²⁸ Our findings are open to interpretation. Although a direct causal link is possible, we cannot exclude the possibility that rhinitis and asthma simply represent the natural progression of a common airway disease. Randomized clinical trials involving treatment of rhinitis to prevent subsequent asthma will be required to determine whether and to what extent rhinitis plays a direct role in the cause of adult-onset asthma.

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