
Correlation between nasal symptoms and asthma severity in patients with atopic and nonatopic asthma

Amin S. Kanani, MD; Irvin Broder, MD; Justina M. Greene; and Susan M. Tarlo, MB,BS

Background: The association between allergic rhinitis and asthma has been well recognized, and it has been postulated that rhinitis may worsen asthma.

Objective: To investigate the severity of asthma among patients with atopic and nonatopic asthma with and without nasal symptoms.

Methods: Atopic asthmatic patients and nonatopic asthmatic patients were identified from the records of a university-based asthma clinic. A comparison of demographic clinical features was made within and between these 2 asthmatic groups, dichotomized according to the presence or absence of rhinitis.

Results: A total of 178 patients were classified as having atopic asthma and 218 as having nonatopic asthma. The atopic asthmatic patients with nasal symptoms compared with those without had a higher mean forced expiratory volume in 1 second (FEV₁), a higher forced vital capacity (FVC), and a higher FEV₁/FVC ratio, used fewer oral steroids, and had fewer hospitalizations. The nonatopic asthmatic patients with nasal symptoms compared with those without used more inhaled steroids (and they were also more likely to have nasal polyps on examination). Atopic, relative to nonatopic, asthmatic patients were younger, had a longer duration of asthma, had a higher FEV₁/FVC ratio, and took fewer oral steroids.

Conclusion: Contrary to current hypotheses, in this study the severity of asthma among atopic asthmatic patients was less in those with nasal symptoms. Conversely, among the nonatopic asthmatic patients, asthma was more severe among those with nasal symptoms than those without nasal symptoms.

Ann Allergy Asthma Immunol. 2005;94:341–347.

INTRODUCTION

The association between allergic rhinitis and asthma has been well recognized,^{1,2} and the incidence of both conditions has been increasing.³ Epidemiologic studies have shown that 20% to 50% of individuals with allergic rhinitis have asthma¹ and 15% to 50% of individuals with asthma have allergic rhinitis.^{4,5} A population study in Tecumseh, MI, reported in 1962 that 29% of individuals with allergic rhinitis have asthma and 45% of individuals with asthma have allergic rhinitis.⁶ Approximately 74% of individuals with asthma and rhinitis developed their rhinitis before or in the same year as their asthma.⁶ The relationship between rhinitis and asthma is unresolved as to whether they are 2 distinct entities or the same disease involving both upper and lower airways. Allergic rhinitis may be a predisposing risk factor for the development of asthma. Uncertainty exists as to whether having allergic rhinitis leads to more severe asthma. Some studies have suggested that nasal symptoms tend to worsen asthma symptoms.^{7,8} In this study, we investigate the severity of asthma in patients with atopic and nonatopic asthma with and

without nasal symptoms, using a previously established detailed patient database with concurrent data.⁹

METHODS

Data obtained at the time of the first clinic visit from the records of 603 asthmatic patients who sought care at the Gage Research Institute during a 10-year period from 1972 were reviewed for this study. The patients were mainly referred by family physicians within a 100-km radius of Toronto, Ontario. All patients were evaluated by clinical immunologists and respirologists from teaching hospitals affiliated with the Faculty of Medicine of the University of Toronto. A standardized format was used, which consisted of a medical questionnaire that included information on current and previous nasal and respiratory symptoms, triggers, medications and other severity indicators, physical examination, skin tests, pulmonary function tests, and laboratory blood tests (eosinophil count and serum IgE), as previously described.⁹ Spirometric results were expressed as the percentage of normal predicted values with use of the prediction formula of Schoenberg et al.¹⁰ Throughout the data collection period (starting in 1972), to maintain testing consistency, intradermal skin tests were performed with the following 8 common allergen extracts (Hollister Stier Laboratories, Toronto, Ontario): house dust mixture (1,000 PNU/mL), *Dermatophagoides pteronyssinus* (1/5,000 wt/vol), tree pollen mix (500 PNU/mL), grass pollen mix (500 PNU/mL), ragweed pollen

Gage Occupational and Environmental Health Unit and Departments of Medicine and Public Health Sciences, University of Toronto, Ontario, Canada.

Received for publication March 15, 2004.

Accepted for publication in revised form July 28, 2004.

Table 1. Characteristics of Atopic Asthmatic Patients (n = 178)

Characteristic	Nasal symptoms (n = 139)	No nasal symptoms (n = 39)	Unadjusted <i>P</i> value (adjusted <i>P</i> value)
Age, mean $\pm$ SD, y	34.8 $\pm$ 13.8	43.7 $\pm$ 15.5	.002
Male, %	51.8	52.5	.94
Nonsmoker, %	52.5	40	.41
Pack-years of smoking, mean $\pm$ SD	7.2 $\pm$ 17.5	10.25 $\pm$ 15.8	.32
Duration of asthma, mean $\pm$ SD, y	17.4 $\pm$ 13.2	22.1 $\pm$ 17	.11
Age of asthma onset, mean $\pm$ SD, y	17.4 $\pm$ 16.5	21.6 $\pm$ 18.9	.16
Peripheral eosinophil count, mean $\pm$ SD	375.3 $\pm$ 351.6	233.6 $\pm$ 245.0	.02 (.14)
IgE, mean $\pm$ SD, IU/mL	567 $\pm$ 770	542 $\pm$ 694	.86
Nasal polyps on examination, %	6.5	2.5	.28
Aspirin sensitive, %	6.5	2.5	.34
Eczema ever, %	23	17.5	.47
Family history of asthma, %	61.2	57.5	.65
Family history of hay fever, %	56.1	37.5	.04 (.09)
FEV ₁ , mean $\pm$ SD, %*	77.3 $\pm$ 25.1	56.6 $\pm$ 21.2	<.001 (<.001)
FVC, mean $\pm$ SD, %	95.7 $\pm$ 20.8	84.1 $\pm$ 19.8	.004 (.01)
FEV ₁ /FVC, mean $\pm$ SD	0.64 $\pm$ 0.15	0.53 $\pm$ 0.13	<.001 (<.001)
Bronchodilator, mean $\pm$ SD, d/y	142.1 $\pm$ 149.2	161.1 $\pm$ 160.3	.50
Bronchodilator currently, %	56.1	65	.33
Inhaled steroid, mean $\pm$ SD, d/y	29.6 $\pm$ 87.5	41.5 $\pm$ 104.3	.47
Inhaled steroid currently, %	15.8	15	.91
Oral steroid, mean $\pm$ SD, d/y	48.3 $\pm$ 110.7	145.2 $\pm$ 169.2	.001 (.003)
Oral steroid currently, %	17.3	52.5	<.001 (<.001)
Hospitalizations, mean $\pm$ SD, No./y	0.2 $\pm$ 0.5	0.6 $\pm$ 1	.02 (.01)
Emergency department visits, mean $\pm$ SD, No./y	0.7 $\pm$ 2.2	2.8 $\pm$ 9.5	.20 (.02)
Physician visits, mean $\pm$ SD, No./y	3.3 $\pm$ 5.4	5.6 $\pm$ 7.1	.06

Abbreviations: FCV, forced vital capacity; FEV₁, forced expiratory volume in 1 second.

*All pulmonary function test results are expressed as percentage of normal predicted values. Adjusted *P* values correct for differences in age, duration of asthma, and smoking pack-years and are shown when different from uncorrected values.

mix (500 PNU/mL), *Cladosporium* (1,000 PNU/mL), *Alternaria tenuis* (1,000 PNU/mL), and feather mix (1,000 PNU/mL). A ninth test was performed with a control solution. The results were read after 20 minutes. Responses were graded relative to the control response as negative (a mean wheal diameter smaller than or equal to the control response), 1+ (1 to 5 mm), 2+ (6 to 9 mm), 3+ ($\geq$ 10 mm), or 4+ (wheal >10 mm and with the presence of pseudopodia). The patients were considered to have asthma if their history, physical examination, and spirometric test results were consistent with episodic obstructive airway disease as judged by the evaluating physician.

Only patients with a diagnosis of asthma and who had skin tests performed were selected for the study. These patients were then divided into a clearly atopic group and a group considered likely to be only mildly atopic or nonatopic based on their skin test results (classified for the purpose of this study as nonatopic). To minimize the likelihood of false-positive skin test responses, at least 1 skin test result of 4+ was required for the patient to be considered atopic and all skin test responses of 2+ or less placed the patient in the nonatopic group for this study. Patients with 1 or more skin test result of 3+ but no response greater than this were considered of intermediate classification and were excluded from the study. The atopic and nonatopic groups were then

divided into those with and without nasal symptoms. To be classified as having nasal symptoms, a patient would have to report 1 or more of the following: nasal discharge, nasal congestion, postnasal drip, and sneezing.

Statistical analysis was performed with SAS statistical software, version 8 (SAS Institute Inc, Cary, NC). The tests performed included χ^2 and *t* tests. *P* values for differences between groups were also calculated with adjustments made for age, smoking pack-years, and duration of asthma, where these were significantly different among compared groups, using the general linear model procedure for continuous variables and the categorical model procedure for categorical variables.

RESULTS

Atopic Group

A total of 178 patients fulfilled our criteria for having atopic asthma. Among these, 71 had a single skin test response considered to be definitely positive (4+), 66 had 2 positive responses, 23 had 3, 12 had 4, and 6 had more than 4 positive (4+) skin test responses. The most common positive response was to dust (103 patients), but all except 29 of these had a 4+ skin test response to at least 1 other allergen extract. Among the 178 atopic patients, extract of *D pteronyssinus*

Table 2. Characteristics of Nonatopic Asthmatic Patients (n = 218)

Characteristics	Nasal symptoms (n = 150)	No nasal symptoms (n = 68)	P value
Age, mean $\pm$ SD, y	49.8 $\pm$ 15	51.8 $\pm$ 13.4	.35
Male, %	51.3	56.5	.47
Nonsmoker, %	41.6	44.9	.74
Pack-years of smoking, mean $\pm$ SD	12.9 $\pm$ 16.8	18.0 $\pm$ 24.5	.12
Duration of asthma, mean $\pm$ SD, y	12.4 $\pm$ 14.4	13.8 $\pm$ 15.8	.55
Age of asthma onset, mean $\pm$ SD, y	37.4 $\pm$ 19.6	37.7 $\pm$ 18.3	.89
Peripheral eosinophil count, mean $\pm$ SD	472.6 $\pm$ 710.6	229.6 $\pm$ 287.5	.007
IgE, mean $\pm$ SD, IU/mL	179.5 $\pm$ 221	90.7 $\pm$ 116	.007
Nasal polyps on examination, %	15.3	1.5	.002
Aspirin sensitive, %	9.2	3	.10
Eczema ever, %	7.8	5.8	.59
Family history of asthma, %	47.7	29	.009
Family history of hay fever, %	31.4	33.3	.77
FEV ₁ , mean $\pm$ SD, %*	70.1 $\pm$ 26.7	67 $\pm$ 30.1	.46
FVC, mean $\pm$ SD, %	92.1 $\pm$ 21.4	89.7 $\pm$ 26.9	.51
FEV ₁ /FVC, mean $\pm$ SD	0.59 $\pm$ 0.15	0.57 $\pm$ 0.16	.37
Bronchodilator, mean $\pm$ SD, d/y	162.4 $\pm$ 154	124.8 $\pm$ 147.6	.09
Bronchodilator currently, %	57.8	49.3	.24
Inhaled steroid, mean $\pm$ SD, d/y	53.3 $\pm$ 118.4	24.1 $\pm$ 75.3	.03
Inhaled steroids currently, %	24.0	10.1	.02
Oral steroid, mean $\pm$ SD, d/y	115.3 $\pm$ 148	117.5 $\pm$ 151.6	.92
Oral steroid currently, %	35.7	47.8	.09
Hospitalizations, mean $\pm$ SD, No./y	0.5 $\pm$ 1	0.4 $\pm$ 0.8	.57
Emergency department visits, mean $\pm$ SD, No./y	0.91 $\pm$ 3.1	0.6 $\pm$ 1.2	.28
Physician visits, mean $\pm$ SD, No./y	4.6 $\pm$ 7.2	5.4 $\pm$ 7.8	.47

Abbreviations: FCV, forced vital capacity; FEV₁, forced expiratory volume in 1 second.

*All pulmonary function test results are expressed as percentage of normal predicted values.

was positive in 57 patients, tree pollen in 20, grass pollen in 58, ragweed pollen in 63, *Alternaria* in 37, *Cladosporium* in 8, and feathers in 10. One hundred thirty-nine (78%) of these atopic patients had nasal symptoms, and 39 (22%) had no nasal symptoms. Among those with nasal symptoms, 78% reported nasal discharge, 77% stuffiness, 73% sneezing, and 57% postnasal drip. Perennial nasal symptoms were reported by 75% of those with nasal symptoms. "Hay fever" was reported by 64%. The mean age of onset of nasal symptoms was 17 years. The baseline characteristics of these patients showed that those with nasal symptoms were significantly younger, had higher peripheral blood eosinophil counts, and had a higher frequency of family members with "hay fever" (Table 1) compared with those without nasal symptoms. Patients with nasal symptoms compared with those without had a higher mean percent predicted forced expiratory volume in 1 second (FEV₁) (77.3% $\pm$ 25.1% vs 56.6% $\pm$ 21.2%, $P < .001$), a higher percent predicted forced vital capacity (FVC) (95.7% $\pm$ 20.8% vs 84.1% $\pm$ 19.8%, $P = .004$), and a higher FEV₁/FVC ratio (0.64 $\pm$ 0.15 vs 0.53 $\pm$ 0.13, $P < .001$). In addition, the patients with nasal symptoms used fewer oral steroids (48.3 $\pm$ 110.7 days per year vs 145.2 $\pm$ 169.2 days per year, $P = .001$) and were less likely to be taking oral steroids for asthma at the time of the visit (17.3% vs 52.5%, $P < .001$) than those without nasal symptoms. Finally, the patients with nasal symptoms had fewer hospi-

talizations (0.2 $\pm$ 0.5 times per year vs 0.6 $\pm$ 1.0 times per year, $P = .02$) than those without nasal symptoms. Adjusting for the significant differences in age and for smoking and duration of asthma did not appreciably change the other significant differences between groups, although differences in eosinophil count were no longer significant (Table 1).

Nonatopic Group

A total of 218 patients were classified for this study as having nonatopic asthma. In this nonatopic asthma group, 84 patients had all skin test results graded as 0, 52 had 1 or more skin test result of 1+ but none greater, and 82 had 1 or more skin test result of 2+ but none greater. One hundred fifty (69%) had nasal symptoms, and 68 (31%) had no nasal symptoms. Among those with nasal symptoms, 73% reported nasal discharge, 68% stuffiness, 54% sneezing, and 54% postnasal drip. The mean age of onset of nasal symptoms was 33 years. Perennial nasal symptoms were reported by 91% of those with nasal symptoms. Sneezing was significantly less common than among atopic asthmatic patients with nasal symptoms ($P < .001$) as was a self-reported history of "hay fever," which occurred in 15% of the nonatopic asthmatic patients with nasal symptoms ($P < .001$). There was no difference in mean age, sex, smoking history, or duration of asthma between the nonatopic asthmatic patients with vs without nasal symptoms. Higher peripheral blood eosinophil counts and

Table 3. Characteristics of All Nonatopic vs Atopic Asthmatic Patients

Characteristics	Nonatopic (n = 28)	Atopic (n = 178)	Unadjusted <i>P</i> value (adjusted <i>P</i> value)
Mean age, y	50.3	36.6	<.001
Male, %	53.2	51.7	.69
Nonsmoker, %	41.9	46.7	.29
Pack-years of smoking, mean $\pm$ SD	14.5 $\pm$ 19.7	7.7 $\pm$ 17.1	<.001
Duration of asthma, mean $\pm$ SD, y	12.8 $\pm$ 14.9	18.3 $\pm$ 14.2	<.001
Age of asthma onset, mean $\pm$ SD, y	37.6 $\pm$ 19.1	18.3 $\pm$ 17.1	<.001
Peripheral eosinophil count, mean $\pm$ SD	397.9 $\pm$ 621.7	348.1 $\pm$ 336.3	.32
IgE, mean $\pm$ SD, IU/mL	197.8 $\pm$ 606.1	633.7 $\pm$ 1032.3	<.001 (<.001)
Nasal polyps on examination, %	10.6	6.2	.06
Aspirin sensitive, %	7.3	5.6	.50
Eczema ever, %	7.2	21.7	<.001 (.05)
Hay fever, %	12	53	<.001 (.001)
Family history of asthma, %	41.6	60.6	<.001 (.02)
Family history of hay fever, %	31.7	52.2	<.001 (.02)
FEV ₁ , mean $\pm$ SD, %*	69.3 $\pm$ 27.8	72.7 $\pm$ 25.7	.20 (.02)
FVC, mean $\pm$ SD, %	91.4 $\pm$ 23.2	93.1 $\pm$ 21	.45
FEV ₁ /FVC, mean $\pm$ SD	0.58 $\pm$ 0.15	0.62 $\pm$ 0.15	.02 (.004)
Bronchodilator, mean $\pm$ SD, d/y	150.2 $\pm$ 152.7	147.6 $\pm$ 151.9	.86
Bronchodilator currently, %	54.9	58.3	.49
Inhaled steroid, mean $\pm$ SD, d/y	44 $\pm$ 107.5	34.1 $\pm$ 94.4	.33
Inhaled steroids currently, %	19.6	16.1	.36
Oral steroid, mean $\pm$ SD, d/y	115.5 $\pm$ 148.7	71.6 $\pm$ 133.4	.002 (.23)
Oral steroid currently, %	39.3	25.6	.004 (.25)
Hospitalization, mean $\pm$ SD, No./y	0.43 $\pm$ 0.95	0.31 $\pm$ 0.69	.14
Emergency department visits, mean $\pm$ SD, No./y	0.81 $\pm$ 2.62	1.24 $\pm$ 5.04	.30
Physician visits, mean $\pm$ SD, No./y	4.84 $\pm$ 7.41	3.84 $\pm$ 5.85	.13

Abbreviations: FCV, forced vital capacity; FEV₁, forced expiratory volume in 1 second.

*All pulmonary function test results are expressed as percentage of normal predicted values. Adjusted *P* values correct for differences in duration of asthma and smoking pack-years and are shown when different from uncorrected values.

serum IgE levels were found in those with nasal symptoms and a greater frequency of family members with asthma in those with nasal symptoms (Table 2). In addition, the patients with nasal symptoms were more likely to have nasal polyps on physical examination (15.3% vs 1.5%, *P* = .002) (Table 2). Patients with nasal symptoms used more inhaled steroids for asthma (53.3 $\pm$ 118.4 days per year vs 24.1 $\pm$ 75.3 days per year, *P* = .03) and were more likely to be taking inhaled steroids for asthma at the time of their visit (24.0% vs 10.1%, *P* = .02) (Table 2).

Comparisons of Atopic and Nonatopic Groups

The 218 nonatopic patients when compared with the 178 atopic patients had an older mean age (Table 3) and a shorter mean duration of asthma. They were less likely to have a history of eczema and hay fever and had less family history of hay fever and asthma. In addition, the nonatopic individuals had a greater smoking history. They had a lower FEV₁/FVC ratio, used more oral steroids, and were more likely to be taking oral steroids at the time of their visit (Table 3). After adjusting for age, smoking, and duration of asthma, significant differences remained between the groups for mean serum IgE antibody levels (*P* < .001), personal history of eczema (*P* = .05), hay fever (*P* < .001), and a family history

of hay fever (*P* = .02) and asthma (*P* = .02), all of which were more common in the atopic group. The mean FEV₁ and FEV₁/FVC ratio were significantly lower in the nonatopic group after adjustment for duration of asthma and smoking history. No significant differences existed in these 2 groups for other markers of asthma severity after adjustment for age, smoking history, and duration of asthma (Table 3).

Comparisons of Atopic and Nonatopic Asthmatic Patients With Nasal Symptoms

Atopic asthmatic patients with nasal symptoms were younger but had a longer duration of asthma than nonatopic asthmatic patients with nasal symptoms. The age of onset of nasal symptoms was significantly lower in the atopic group (17.3 $\pm$ 12.2 years vs 32.9 $\pm$ 16.2 years, *P* < .001). Nasal symptoms were more likely to be only seasonal in the atopic group vs the nonatopic group with nasal symptoms (25% vs 8.5%, *P* < .001). As in the total groups, the nonatopic asthmatic patients with nasal symptoms had a greater smoking history than the atopic asthmatic patients with nasal symptoms. Markers of asthma severity were greater among the nonatopic group with nasal symptoms than among the atopic group (Table 4), and after adjustment for differences in age, smoking, and duration of asthma, significant differences

Table 4. Measures of Severity in Nonatopic vs Atopic Asthmatic Patients With Nasal Symptoms

Measure	Nonatopic (n = 150)	Atopic (n = 139)	Unadjusted <i>P</i> value (adjusted <i>P</i> value)
FEV ₁ , mean ± SD, %*	70.1 ± 26.7	77.3 ± 25.1	.02 (.008)
FVC, mean ± SD, %	92.1 ± 21.4	95.7 ± 20.8	.15
FEV ₁ /FVC, mean ± SD	0.59 ± 0.15	0.64 ± 0.15	.002 (<.001)
Bronchodilator, mean ± SD, d/y	162.4 ± 154	142.1 ± 149.2	.25 (.006)
Bronchodilator currently, %	57.8	56.1	.77
Inhaled steroid, mean ± SD, d/y	53.3 ± 118.4	29.6 ± 87.5	.05 (.08)
Inhaled steroids currently, %	24.0	15.8	.08
Oral steroid, mean ± SD, d/y	115.3 ± 148	48.3 ± 110.7	<.001 (.008)
Oral steroid currently, %	35.7	17.3	<.001 (.04)
Hospitalizations, mean ± SD, No./y	0.5 ± 1	0.2 ± 0.5	.01 (.05)
Emergency department visits, mean ± SD, No./y	0.91 ± 3.1	0.7 ± 2.2	.47
Physician visits, mean ± SD, No./y	4.6 ± 7.2	3.3 ± 5.4	.08

Abbreviations: FCV, forced vital capacity; FEV₁, forced expiratory volume in 1 second.

*All pulmonary function test results are expressed as percentage of normal predicted values. Adjusted *P* values corrected for differences in duration of asthma and smoking pack-years and are shown when different from uncorrected values.

Table 5. Measures of Severity in Nonatopic vs Atopic Asthmatic Patients Without Nasal Symptoms

Measure	Nonatopic (n = 68)	Atopic (n = 39)	Unadjusted <i>P</i> value (adjusted <i>P</i> value)
FEV ₁ , mean ± SD, %*	67 ± 36.2	56.6 ± 21.2	.04 (.16)
FVC, mean ± SD, %	89.6 ± 26.9	84.1 ± 19.8	.23
FEV ₁ /FVC, mean ± SD	0.57 ± 0.16	0.53 ± 0.13	.20
Bronchodilator, mean ± SD, d/y	124.8 ± 148	161.1 ± 160.3	.24
Bronchodilator currently, %	49.3	65	.12
Inhaled steroid, mean ± SD, d/y	24.1 ± 75.3	41.4 ± 104.3	.39
Inhaled steroids currently, %	10.1	15.0	.45
Oral steroid, mean ± SD, d/y	117.45 ± 151.6	145.2 ± 169.2	.36
Oral steroid currently, %	47.8	52.5	.64
Hospitalizations, mean ± SD, No./y	0.38 ± 0.75	0.61 ± 0.99	.21
Emergency department visits, mean ± SD, No./y	0.60 ± 1.22	2.78 ± 9.46	.16
Physician visits, mean ± SD, No./y	5.4 ± 7.8	5.6 ± 7.1	.87

Abbreviations: FCV, forced vital capacity; FEV₁, forced expiratory volume in 1 second.

*All pulmonary function test results are expressed as percentage of normal predicted values. Adjusted *P* values correct for differences in duration of asthma and smoking pack-years and are shown when different from uncorrected values.

were present for a lower FEV₁ and FEV₁/FVC ratio, greater reported use of inhaled bronchodilators, more days of oral steroid use for asthma, and greater number of hospital admissions for asthma among nonatopic asthmatic patients with nasal symptoms compared with atopic asthmatic patients with nasal symptoms.

In contrast, no significant differences occurred in severity markers between atopic and nonatopic asthmatic patients without nasal symptoms on univariate analyses except for a reduced FEV₁ (Table 5) and a trend to more severe asthma in the atopic vs nonatopic asthmatic patients without nasal symptoms. Adjustment for group differences in age, smoking, and duration of asthma resulted in loss of the statistical difference in FEV₁.

DISCUSSION

In the atopic asthmatic patients in this study, markers of severity of asthma were greater in patients without nasal

symptoms than in those with nasal symptoms. Conversely, in the nonatopic group, the patients with nasal symptoms reported more use of inhaled steroids for asthma than those without nasal symptoms. When comparing the entire atopic asthmatic group with the nonatopic asthmatic group, regardless of their nasal symptoms, the nonatopic group tended to have more severe asthma as evaluated by spirometry, medication use, and medical services used. However, the nonatopic group of asthmatic patients was significantly older and had a shorter mean duration of asthma. Other than a lower FEV₁ in the nonatopic group, the differences in asthma severity between the atopic and nonatopic asthmatic groups were no longer significant when adjusted for age and duration of asthma, as we have previously reported.⁹ The population in the present study was derived from the same data set from which more definite atopic vs nonatopic groups have previously been examined by us,⁹ with similar conclusions as to differences in severity between atopic and nonatopic asth-

matic patients. The data collection started 30 years ago, and although management of asthma has changed since this time, it is not likely that the differences observed in the present analyses would be influenced by these changes.

Atopy was determined by intradermal skin test. Intradermal skin testing was a standard method of determining atopy at the time when asthma patients were initially being evaluated at the Gage Research Institute during the beginning of this data collection period and was continued during this 10-year period (to 1982) to maintain consistency. Testing using the intradermal method has a high sensitivity but lower specificity than skin prick testing.^{11,12} To avoid false-positive results, we chose an intradermal test result of 4+ to represent atopy, similar to our previous analyses.⁹ We considered 1+ or 2+ responses to be nonatopic, recognizing that some may actually have been mildly atopic. Despite the inclusion of asthmatic patients with 1+ and 2+ skin test responses in the nonatopic group in the present analyses, the mean age, sex, and duration of asthma of the 218 patients in this nonatopic group are almost identical to the 71 patients with completely negative skin test results described in our earlier report.⁹ Also, the same differences between the entire atopic vs nonatopic asthmatic groups were found in the present analyses as in our earlier study, suggesting that the inclusion of the 1+ and 2+ skin test responses in the nonatopic group did not likely bias the present results. Similarly, although some positive intradermal skin test responses, particularly smaller responses, can reflect irritation rather than true IgE antibody responses, only 6 patients had more than 4 of 8 positive skin test results, suggesting that it was unlikely that the skin test solutions were causing general irritant responses. In particular, although the dust extract that might be expected to induce nonspecific responses from endotoxin or other irritants was the most common positive extract on skin testing, nevertheless only 29 of the total 179 patients with positive skin test results responded solely to this extract with a 4+ response (data not shown). In addition, the group differences in characteristics, such as total serum IgE level and history of eczema or hay fever (Table 3), are in support of atopic vs nonatopic groups. Therefore, we consider it unlikely that the intradermal test with the classifications used in this study resulted in significantly false groupings of patients.

Contrary to what has been suggested, the severity of asthma in the atopic group tended to be greater in patients without nasal symptoms than those with nasal symptoms, based on spirometry, steroid use, and hospital admissions. This study did not include other asthma control assessments, such as peak flow variability, measures of airway hyperresponsiveness, or asthma control days, which would be useful to include in prospective studies in the future, as would information as to other possible comorbidity confounders, such as the presence of gastroesophageal reflux. Several editorials and reviews have discussed the association between rhinitis and asthma,^{1,13-16} but there have been few studies that directly assessed this association.^{2,7,8} In a study by Huse et al,⁷ a correlation between asthma severity and allergic rhinitis

was observed. In addition, Corren et al¹⁷ reported that in patients with asthma, treatment of concomitant allergic rhinitis was associated with reduced risk of emergency department visits and hospitalization for asthma. However, spirometry values and the incidence of nasal polyps were not mentioned. Halpern et al⁸ showed that health care costs were higher for patients with asthma and rhinitis than asthma alone but did not distinguish between atopic and nonatopic asthmatic patients.

Atopic asthmatic patients without nasal symptoms may have different mechanisms that contribute to the severity of their asthma than those with nasal symptoms. For example, in some atopic asthmatic patients, particularly those without nasal symptoms, the presence of atopy as defined by skin testing may be a coincidental finding and the asthma pathogenesis may be more similar to that of nonatopic asthmatic patients. This would be in keeping with our finding that the atopic asthmatic patients without nasal symptoms had a mean age almost 10 years older than the atopic asthmatic patients with nasal symptoms ($P = .002$), similar to the mean age of the nonatopic asthmatic group, and mean eosinophil counts and IgE antibody levels were lower than in the atopic asthmatic patients with nasal symptoms, suggesting a lower level of expression of these features of atopy compared with the atopic asthmatic patients with nasal symptoms.

Nevertheless, it is difficult to clearly explain the apparent findings of milder asthma in the atopic asthmatic patients with nasal symptoms. They might have had some improvement in asthma symptoms from nasal steroids, although this was not generally available in the period of the study. It is possible that patients with milder asthma with nasal symptoms sought medical attention in this secondary or tertiary referral center in part due to concurrent nasal symptoms. This could be further evaluated by studies in primary care settings. The atopic asthmatic patients with no nasal symptoms had a significantly greater use of oral steroids, which could potentially have reduced or cleared nasal symptoms to the extent that they were not reported. Therefore, it is possible that these patients, considered as having a greater severity of asthma, may be placed in the group without nasal symptoms. We believe, however, that this may apply to only a few individuals, because most patients in the atopic group reported nasal symptoms (139 vs 39). Finally, it is possible that there may have been confounding factors such as gastroesophageal reflux, which was not objectively evaluated in this study and which might have played a role in upper or lower respiratory tract symptoms.

The upper airway can affect the lower airway in many ways, including nasal obstruction that causes mouth breathing and bypass of nasal passages, nasobronchial reflex, or propagation of inflammation from the upper to the lower airway directly or via the systemic circulation.¹⁶ Several studies have demonstrated that use of intranasal steroids in patients with nasal symptoms can also improve control of asthma.¹⁵⁻²² All but one of these studies²² did not exclude the possibility that the nasal steroids may be concurrently inhaled

into the lower airways through the nose, and as noted herein this might have resulted in findings of milder asthma.

In nonatopic asthmatic individuals a strong relationship between perennial nasal symptoms and asthma has already been demonstrated.²³ Our study confirms the finding that nonatopic asthmatic individuals with nasal symptoms had more severe asthma than those without nasal symptoms, with an increased number of days using an inhaled steroid and an increased likelihood of using an inhaled steroid at the time of their visit. The nonatopic asthmatic patients with nasal symptoms also had a higher incidence of nasal polyps, which may relate to their increase in asthma severity, perhaps through an increased eosinophilic inflammatory response. When patients with nasal polyps were removed from the analyses of the nonatopic group, the only difference discovered between the nonatopic asthmatic patients with and without nasal symptoms was that those with nasal symptoms were taking inhaled steroids for a greater number of days.

Although a relationship between rhinitis and asthma has been well recognized, this study had some unexpected findings when assessing the severity of asthma within groups of atopic and nonatopic asthmatic individuals with and without nasal symptoms. Further investigations are required to better understand the relationship between rhinitis and asthma, particularly by separating atopic and nonatopic groups.

REFERENCES

1. Guerra S, Sherrill DL, Martinez FD, Barbee RA. Rhinitis as an independent risk factor for adult-onset asthma. *J Allergy Clin Immunol.* 2002;109:419–425.
2. Bousquet J, Vignola AM, Demoly P. Links between rhinitis and asthma. *Allergy.* 2003;58:691–706.
3. Ninan TK, Russell G. Respiratory symptoms and atopy in Aberdeen school children: evidence from two surveys 25 years apart. *BMJ.* 1992;304:873–875.
4. Scadding GK. The co-existence of upper and lower airways disease. *Respir Dis Pract.* 1994;11:18–20.
5. Braman SS, Barrows AA, De Cotiis BA, et al. Airway hyper-responsiveness in allergic rhinitis: a risk factor for asthma. *Chest.* 1987;91:671–674.
6. Broder I, Barlow PP, Horton RJ. The epidemiology of asthma and hay fever in a total community, Tecumseh, Michigan, II: the relationship between asthma and hay fever. *J Allergy.* 1962;33: 514–531.
7. Huse DM, Hartz SC, Klaus DH, et al. Does allergic rhinitis exacerbate asthma symptoms in adults? the asthma outcomes registry [abstract]. *Eur Respir J.* 1996;9:351s.
8. Halpern M, Richner R, Togias A, et al. Allergic rhinitis may increase asthma costs [abstract]. *Am J Respir Crit Care Med.* 1996;153:A860.
9. Inouye T, Tarlo S, Broder I, et al. Severity of asthma in skin test-negative and skin test-positive patients. *J Allergy Clin Immunol.* 1985;75:313–319.
10. Schoenberg JB, Beck GJ, Bouhuys A. Growth and decay of pulmonary function in healthy blacks and whites. *Respir Physiol.* 1978;33:367.
11. Bernstein IL, Storms WW; Joint Task Force on Practice Parameters for the Diagnosis and Treatment of Asthma, American Academy of Allergy Asthma and Immunology and the American College of Allergy Asthma and Immunology. Practice parameters for allergic diagnostic testing. *Ann Allergy Asthma Immunol.* 1995;75:543–625.
12. American Academy of Allergy Asthma and Immunology Board of Directors. Allergen skin testing [position paper]. *J Allergy Clin Immunol.* 1993;92:636–637.
13. Simons EF. Allergic rhinobronchitis: the asthma-allergic rhinitis link. *J Allergy Clin Immunol.* 1999;104:534–540.
14. Scadding GK. Could treating asthma help rhinitis? *Clin Exp Allergy.* 1997;27:1387–1393.
15. De Benedictis FM, Bush A. Rhinosinusitis and asthma epiphenomenon or casual association? *Chest.* 1999;115:550–556.
16. Togias A. Rhinitis and asthma: evidence for respiratory system integration. *J Allergy Clin Immunol.* 2003;111:1171–1183.
17. Corren J, Manning BE, Thompson SF, Hennessy S, Strom B. Rhinitis therapy and the prevention of hospital care for asthma. *J Allergy Clin Immunol.* 2004;113:415–419.
18. Reed CE, Marcoux JP, Welsh PW. Effects of topical nasal treatment on asthma symptoms. *J Allergy Clin Immunol.* 1998; 81:1042–1047.
19. Corren J, Adinoff AD, Buchmeier AD, Irvin CG. Nasal beclomethasone prevents the seasonal increase in bronchial responsiveness in patients with allergic rhinitis and asthma. *J Allergy Clin Immunol.* 1992;90:250–256.
20. Foresi A, Pelucchi A, Gherson G, et al. Once daily intranasal fluticasone propionate reduces nasal symptoms and inflammation but also attenuates the increase in bronchial responsiveness during the pollen season in allergic rhinitis. *J Allergy Clin Immunol.* 1996;98:274–282.
21. Henriksen JM, Wenzel A. Effect of an intranasally administered corticosteroid (budesonide) on nasal obstruction, mouth breathing, and asthma. *Am Rev Respir Dis.* 1984;130:1014–1018.
22. Watson WTA, Becker AB, Simons FER. Treatment of allergic rhinitis with intranasal corticosteroids in patients with mild asthma: effect on lower airway responsiveness. *J Allergy Clin Immunol.* 1993;91:97–101.
23. Leynaert B, Bousquet J, Neukirch C, et al. Perennial rhinitis: an independent risk factor for asthma in nonatopic subjects: results from the European Community Respiratory Health Survey. *J Allergy Clin Immunol.* 1999;104:301–304.

Requests for reprints should be addressed to:
Susan M. Tarlo, MB,BS
Gage Occupational and Environmental Health Unit
223 College St
Toronto, Ontario
M5T 1R4 Canada
E-mail: susan.tarlo@utoronto.ca