

Coexistence of Asthma and Allergic Rhinitis in Adult Patients Attending Allergy Clinics: ONEAIR Study

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■ Abstract

Background: Several studies have shown links between the upper and lower airways in allergic patients.

Objectives: This study aimed to evaluate the prevalence of rhinitis in patients with allergic asthma attending allergy outpatient clinics and to examine the interrelationship between both conditions.

Methods: An epidemiological prospective study was carried out during the period 2004-2005 and 170 allergists from all over the country participated. After obtaining written informed consent, we collected clinical and demographic data, a personal and family history of allergic diseases, and data on the duration and severity of asthma and rhinitis. These data were classified according to the criteria of the Global Initiative for Asthma and the Allergic Rhinitis and its Impact on Asthma guidelines, respectively.

Results: A total of 968 subjects were screened and 942 were enrolled in the study. Mean (SD) age was 35.5 (14) years and 63% were female. Of these patients, 89.5% presented with allergic rhinitis. The duration of the disease was 12.6 (8.9) years for rhinitis and 11.4 (9.6) years for asthma ($P < .0001$). The severity of asthma was classified as intermittent (39%), mild persistent (30%), moderate persistent (27%), and severe persistent (4%). Rhinitis was classified as mild intermittent (24%), moderate/severe intermittent (22%), mild persistent (19%) and moderate/severe persistent (35%). A significant correlation was found ($P < .0001$) between the severity of rhinitis and asthma. The prevalence of allergic rhinitis was inversely correlated with the age of the patients ($P < .0001$) and the severity of asthma ($P < .05$).

Conclusion: This study reinforces the high prevalence of allergic rhinitis in patients with asthma, which can affect as many as 89.5%.

Key words: Allergic asthma. Allergic rhinitis. Asthma and rhinitis comorbidity.

■ Resumen

Antecedentes: La interrelación entre la vía respiratoria alta y baja en pacientes alérgicos ha sido demostrada en varios estudios.

Objetivos: Evaluar la prevalencia de rinitis en pacientes con asma atendidos en consultas de alergología, así como valorar aspectos de la interrelación entre ambas enfermedades.

Métodos: Estudio epidemiológico prospectivo, realizado en 2004-2005, con la colaboración de 170 alergólogos españoles. Tras obtener el consentimiento informado se recogieron datos personales demográficos y clínicos, antecedentes familiares de atopía, así como información sobre la duración y gravedad del asma y la rinitis, que se clasificaron según el criterio de la GINA y del ARIA, respectivamente.

Resultados: Un total de 968 pacientes fueron seleccionados, de los que 942 fueron incluidos en el estudio, 63% eran mujeres, con edad media (desviación estándar) de 35.5 (14) años. El 89.5% de estos pacientes presentaban rinitis alérgica. El tiempo de evolución fue de 12.6 (8.9) años para rinitis y 11.4 (9.6) años para asma ($P < 0,0001$). Clasificación del asma según la gravedad: intermitente 39%, persistente leve 30%, persistente moderada 27%, y persistente grave 4%. Clasificación de la rinitis: intermitente leve 24%, intermitente moderada/grave 22%, persistente leve 19% y persistente moderada/grave 35%. Se encontró una correlación significativa ($P < 0,0001$) entre la gravedad de la rinitis y del asma. La prevalencia de la rinitis alérgica se correlacionó de forma inversa con la edad de los pacientes ($P < 0,0001$) y la gravedad del asma ($P < 0,05$).

Conclusión: Este estudio corrobora la alta prevalencia de la asociación entre rinitis y asma en pacientes alérgicos, afectando al 89.5% de los pacientes estudiados.

Palabras clave: Asma alérgica. Rinitis alérgica. Comorbilidad asma y rinitis.

Introduction

Asthma and rhinitis have traditionally been considered 2 different nosological entities, affecting the lower and upper airways, respectively. Recent pathophysiological findings, however, have identified both disorders as manifestations of the chronic inflammatory respiratory syndrome of the common airways, or united airways disease [1,2]. Thus, allergic rhinitis or asthma cannot be confined to a specific site, but should be considered a disorder of the whole respiratory tract, with a range of clinical manifestations and relevant diagnostic and therapeutic implications.

Asthma and allergic rhinitis are frequently concurrent diseases. This link has been established in clinical observations and epidemiological studies and also on the basis of immunological observations and outcomes of therapy [3-5].

The frequent coexistence of both diseases and their close interrelationship led the World Health Organization (WHO) and the ARIA Initiative (Allergic Rhinitis and Its Impact on Asthma) to release, in 2001, a comprehensive overview of the pathophysiology, diagnosis, and therapy of allergic rhinitis [2]. The main objectives of this initiative were to update medical knowledge on allergic rhinitis, to emphasize the impact of allergic rhinitis on asthma, and to provide evidence-based diagnostic and therapeutic guidelines.

About 4% to 11% of the general population has asthma, whereas the prevalence of allergic rhinitis is around 10% to 30% [6,7]. Between 20% and 50% of patients with allergic rhinitis have asthma, and 30% to 90% of patients with asthma have concomitant rhinitis [8-10]. The simultaneous presentation of rhinitis and asthma is independent of the etiology of the disorder. Moreover, allergic rhinitis may be a predisposing risk factor for the development of asthma [11] and it has been reported to be a risk factor for both the incidence and severity of allergic asthma [12]. Uncertainty exists, however, as to whether the severity of allergic rhinitis is related to more severe asthma.

The frequent coexistence of asthma and rhinitis means that the presence and severity of allergic rhinitis should be assessed in every patient with asthma. Furthermore, adequate management of both diseases is essential to achieve optimal therapeutic outcomes.

In this study, we evaluate the prevalence of the association between asthma and allergic rhinitis in adult asthmatic patients attending allergy outpatient clinics. We also examine the relationship between both disorders.

Methods

A prospective epidemiological study was carried out during 2004-2005. This study was approved by the Ethics Committee of the Hospital Clínic in Barcelona and 170 allergists from all over Spain participated. Every researcher recruited 6 consecutive patients with asthma attending the allergy outpatient clinics. After obtaining written informed consent, the participating physicians administered a structured questionnaire, which requested demographic data (age, gender, residence), data on exposure to pets or other animals, smoking, personal and family history of

atopy, clinical features of asthma and rhinitis (frequency and severity of the symptoms, exacerbations, duration of the disease). The severity of asthma was classified according to the Global Initiative for Asthma (GINA) report [13] and allergic rhinitis according to ARIA [2]. Skin prick testing was performed in all patients with a panel of the most relevant aeroallergens in each geographical area. Spirometry was carried out according to European Respiratory Society (ERS) standards, and spirometric predicted normal values were based on the reference values from ERS guidelines for adult patients [14].

Statistical Analysis

Statistical tests were performed using variance analysis to compare quantitative variables between 2 or more factors. When several factors were considered (for instance, severity of asthma and rhinitis), a post hoc analysis was performed using the Bonferroni test. To assess the correlation between 2 variables, the Pearson correlation coefficient was used for continuous variables (duration of asthma and rhinitis symptoms) and the Spearman rank correlation coefficient (ρ) for ordinal variables (such as severity of asthma and rhinitis). To evaluate the association between qualitative variables, the chi-square test with an analysis of residues was applied, and the intensity of the association was expressed as the odds ratio (OR) and 95% confidence interval (95% CI). This test was also used in conjunction with the Cuzick trend test to compare the trend of dichotomous variables such as comorbidity through an ordinal variable such as asthma severity.

Results

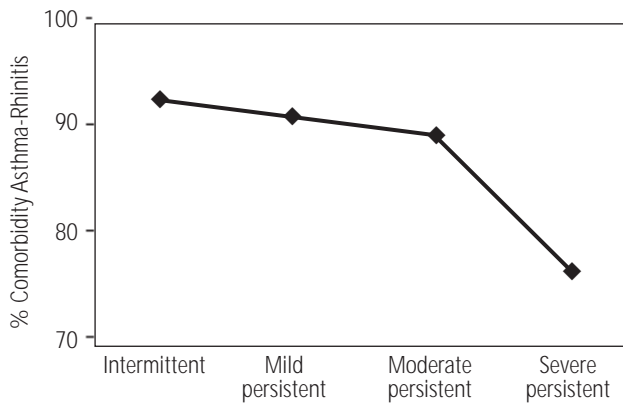
A total of 968 adult subjects were screened. After excluding 26 subjects (2.7%) due to incomplete data collection, 942

Table 1. Demographic and Clinical Characteristics of the Study Population (N = 942)

Age, y	35.5 (14)
Gender	
Female	63%
Male	37%
Nonsmokers	83%
Residence	
Urban	74%
Rural	26%
Exposure to animals	42%
Family history of atopy	
Rhinitis	33%
Asthma	35%
Personal history of atopy	
Atopic dermatitis	10%
Food allergy	7%
Urticaria	4%

subjects (97.3%) with asthma were analyzed. Clinical and demographic data of the study population are shown in Table 1.

Classification of asthma severity in these patients according to GINA is shown in Table 2. Subjects with more severe asthma tend to be older than those with intermittent asthma, particularly in patients with moderate persistent asthma ($P < .0001$) and severe persistent asthma ($P < .001$). A high prevalence of the co-existence of rhinitis was found in patients with intermittent asthma (92%), mild persistent asthma (90%), and moderate persistent asthma (89%), and to a lesser extent in severe persistent asthma (76%). This implies that the more severe the asthma, the less frequent the prevalence of comorbid rhinitis ($P < .05$) (Figure, A).



Figure, A. Types of asthma.

The mean (SD) duration of asthma symptoms was 11.4 (10) years. Statistically significant differences were found in the duration of asthma between the different asthma severity subgroups, and the duration of asthma was longer among patients with more severe asthma. The most pronounced differences were found between patients with intermittent and moderate persistent asthma ($P < .02$).

Concomitant allergic rhinitis affected 89.5% of patients with asthma. According to the frequency of symptoms, allergic rhinitis was classified as intermittent in 46% and persistent in 54% of patients. Severity was stratified as mild in 43% and moderate-persistent in 57% (Table 2).

The mean duration of rhinitis was 12.6 (9) years, and no

Table 2. Classification of Asthma (GINA) and Rhinitis (ARIA) (N = 942)

Asthma Classification	%	Rhinitis Classification	%
Intermittent	39	Mild intermittent	24
Mild persistent	30	Moderate-severe intermittent	22
Moderate persistent	27	Mild persistent	19
Severe persistent	4	Moderate-severe persistent	35

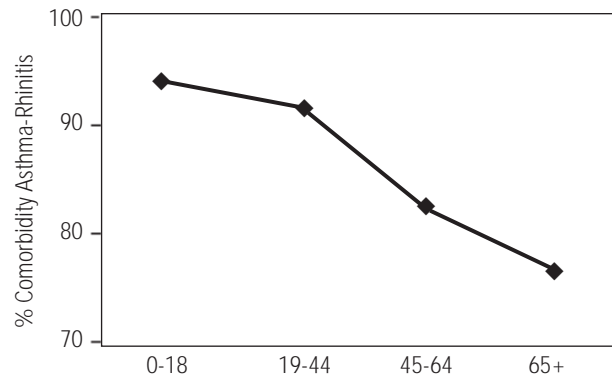
Abbreviations: ARIA, Allergic Rhinitis and Its Impact on Asthma; GINA, Global Initiative for Asthma.

statistically significant differences were observed for rhinitis category or age. A significant positive correlation ($P < .0001$) was found between the severity of rhinitis and asthma.

The prevalence of the comorbidity of asthma and rhinitis fell as age increased ($P < .0001$) (Figure, B).

The duration of rhinitis was longer than that of asthma ($P < .0001$), both for allergic ($P < .001$) and nonallergic patients ($P < .05$). As for symptoms at presentation of the respiratory condition, 36% of patients had rhinitis, 12% had asthma, and 52% had asthma and rhinitis simultaneously.

A family history of rhinitis was a significant risk factor (OR 11.9; 95% CI, 6.9-20.3) for the comorbidity of rhinitis and asthma.



Figure, B. Age, y

No significant differences were found between a rural and urban habitat for the association between rhinitis and asthma and no association was found for exposure to animals or smoking.

According to skin prick testing results, 900 subjects (95.5%) were sensitized to at least 1 aeroallergen: 61.7%

Table 3. Frequency of Positive Skin Prick Tests to Common Aeroallergens (N = 900)

<i>D pteronyssinus</i>	50%
<i>D farinae</i>	42%
<i>Lolium perenne</i>	44%
<i>Olea europaea</i>	39%
Dog dander	30%
Cat dander	29%
<i>Chenopodium album</i>	18%
<i>Parietaria judaica</i>	14%
<i>Artemisia vulgaris</i>	14%
<i>Platanus hybrida</i>	13%
<i>Cupressus arizonica</i>	12%
<i>Alternaria alternata</i>	10%
<i>Cladosporium herbarum</i>	2%

were sensitized to pollen, 51.7% to house dust mites, 39.8% to animal dander, 11.6% to molds, and 1.3% to latex (Table 3). A significant association ($P < .0001$) was found between having a positive skin prick test and experiencing rhinitis, with an OR of 11.9 (95% CI, 6.1-23.3). As for reactivity to individual allergens, a higher prevalence rhinitis and asthma was found in subjects sensitized to pollen or animal dander.

Lung function testing (spirometry) was performed in 742 patients (79%), and was within normal limits in 90%. No significant differences were observed in the spirometric parameters between patients with asthma or with asthma and rhinitis simultaneously.

Discussion

Several results in this study are noteworthy: the high prevalence of allergic rhinitis among patients with asthma (89.5%); the finding that, the older the patients and the more severe the asthma, the lower the prevalence of rhinitis; the positive correlation between the patient's age and duration and severity of asthma; the correlation between the severity of asthma and rhinitis; and the observation that rhinitis usually precedes or starts simultaneously with asthma.

Most epidemiological studies on the interrelationship between rhinitis and asthma have evaluated the prevalence of asthma among subjects suffering from rhinitis, with frequencies ranging from 20% to 50% [15-19], or as high as 70% in a study conducted in young army recruits [20].

The prevalence of allergic rhinitis among subjects with asthma in previous studies varies widely. Recent studies carried out in large population samples report prevalences of between 80% and 95% of patients [5]. In a study carried out in 3916 adults, 82% of subjects with asthma had rhinitis [21]. Some studies point out that the prevalence of rhinitis in adult patients with asthma is as high as 99%, and in young people it can reach 95% [22-24].

We found that the duration of rhinitis was longer than that of asthma ($P < .0001$), and that this was true for both allergic ($P < .001$) and nonallergic subjects ($P < .05$). Moreover, in most cases (88%), rhinitis precedes or is simultaneous with asthma. Several studies show that rhinitis is the first clinical manifestation of chronic allergic respiratory disease, which may subsequently progress to asthma [2,5]. Notwithstanding, asthma and rhinitis can sometimes start simultaneously, or asthma may even precede rhinitis. In a study carried out on 738 students, Greisner et al [25] reported that 45% of subjects with both seasonal rhinitis and asthma developed rhinitis earlier, 35% developed asthma before rhinitis, and 21% experienced both conditions simultaneously. In subjects with perennial rhinitis and asthma, 38% developed rhinitis first, 31% asthma before rhinitis, and 31% both conditions at the same time. Thus, in 70%-80% of cases, allergic rhinitis begins before or at the same time as asthma, which agrees with the figure of 76% reported by Guerra et al [11]. These data further emphasize the link between allergic rhinitis and asthma as manifestations of a common inflammatory airway disorder that often occur together during the natural history of the disease.

The finding that the prevalence of rhinitis decreases with age and asthma severity increases might be because rhinitis can subside during the natural history of chronic airway inflammatory disease, or perhaps because the more pronounced severity of asthma with age may lead to underdiagnosis of rhinitis. There is little information on the possibility of spontaneous remission of allergic rhinitis. During an 8-year follow-up of patients with allergic rhinitis, Nihlen et al [26] found a 20% remission rate, which was higher in older patients and in subjects allergic to pollen. Other studies have also reported the relationship between age and improvement or waning of rhinitis over the years [27,28]. Matsuno et al [24] found that 66% of asthmatic subjects aged less than 60 years suffered from allergic rhinitis, whereas the prevalence was 39% in subjects older than 60 years.

Rhinitis and asthma represent a disorder of the whole respiratory tract, with a range of clinical manifestations at different sites. This syndrome has a spectrum of severity that ranges from rhinitis alone, rhinitis with airway hyperresponsiveness and no asthma symptoms, and the coexistence of equally severe rhinitis and asthma [29]. The characteristics of rhinitis affect the presence and severity of asthma [30]. We found that the older the patient and the longer the duration of disease, the more severe the asthma. This finding, however, was not observed for rhinitis. In this regard, one study has shown that 35.7% of patients experienced a parallel worsening of asthma and rhinitis, whereas in 52.7% rhinitis did not worsen when asthma did [24]. Another study reported that rhinitis is more severe in subjects who had both asthma and rhinitis than in those who only had rhinitis [31].

The severity of rhinitis may also affect the development of asthma. Several studies have confirmed the importance of rhinitis symptoms in the future development of asthma [19]. Subjects with persistent rhinitis and severe rhinitis symptoms had a risk at least 5 times higher of developing asthma [12]. Rhinitis is more severe in subjects who have both asthma and rhinitis than in those who only have rhinitis [23]. A study conducted in children found that the presence of severe rhinitis in those with asthma was associated with higher asthma severity [25]. Another study reported that when allergic rhinitis improved, asthma also improved, whereas the persistence of allergic rhinitis was correlated with the persistence of asthma symptoms [29]. Marogna et al [17], in an epidemiologic study carried out in 832 subjects with intermittent rhinitis, found that 11.6% developed asthma when rhinitis was mild and 22.2% when the condition was moderate-severe ($P < .001$), whereas in 968 subjects who had persistent rhinitis, 30.1% and 35.4% ($P > .05$) developed asthma when rhinitis was mild and moderate-severe, respectively.

Allergic sensitization to aeroallergens seems to be an important risk factor in the association between rhinitis and asthma. Whereas sensitization to domestic allergens is clearly related to the development of asthma, sensitization to pollen alone is particularly associated with rhinitis [32]. In our study, the higher prevalence of the coexistence of rhinitis and asthma was observed in subjects sensitized to pollen and animal dander. Several studies show a higher frequency of the association with rhinitis in patients allergic to house dust mites and animal dander, whereas in rhinitis without concomitant

asthma, sensitization to pollen is more frequent. Asthma without rhinitis is associated with sensitization to domestic allergens, especially to *Alternaria* species in the most severe cases. The risk of suffering from asthma increases by 6.7% among subjects with allergic rhinitis due to pollen and by 11.9% in patients sensitized to indoor allergens (animal dander, mites, and cockroaches). The frequency of asthma among subjects with allergic rhinitis varies according to whether they are exclusively sensitized to cat, house dust mites, molds, and pollen (26.3%, 22.3%, 21.9%, and 15.8%, respectively) [33]. Boulet et al [34] demonstrated that sensitization to indoor allergens was frequently associated with the presence of asthma, whereas sensitization to pollen alone was associated with the presence of rhinitis. Among the subjects sensitized to outdoor allergens, 74% had rhinitis, 14% both asthma and rhinitis, and 12% only asthma; among those sensitized to indoor allergens, 49% had rhinitis, 27% both asthma and rhinitis and 24% asthma. If they were sensitized to both allergen types, the prevalences were 55%, 30%, and 15%, respectively. These data stress the importance of the etiology of rhinitis in the development of asthma.

Different studies have validated the ARIA classification of rhinitis [2]. In our study, 46% of cases were intermittent, 54% persistent, 43% mild, and 57% moderate-severe. Other authors have found disparate results according to the population studied. Demoly et al [35], who studied 6533 subjects attending general medicine, allergy, pulmonology, or ENT outpatient clinics during the spring or fall, found that 49% had intermittent rhinitis and 51% persistent rhinitis. Pereira et al [18], whose study included 3225 subjects attended at allergy clinics, found that 36% had intermittent rhinitis, 64% persistent rhinitis, 59% mild rhinitis, and 41% moderate-severe rhinitis. Bachert et al [36], who studied 554 subjects recruited from the general population with rhinitis symptoms during the previous year, found that 59% had intermittent rhinitis, 41% persistent rhinitis, 25% mild rhinitis, and 75% moderate-persistent rhinitis. Bouquet et al [37] reported that, of 3052 subjects who consulted for rhinitis in primary care, 46% had intermittent rhinitis, 54% persistent rhinitis, 19% mild rhinitis, and 81% moderate-severe disease. These results indicate the existence of considerable differences in the prevalence of the different types of allergic rhinitis according to the characteristics of the study population and the health care context.

In conclusion, our study reveals a high prevalence of comorbidity (89.5%) of allergic rhinitis among patients with asthma. A positive correlation was found between duration and severity of asthma, but this was not observed for rhinitis. The severity of rhinitis tends to parallel that of asthma, and in most cases rhinitis precedes or starts with asthma. The prevalence of the different rhinitis subgroups in the ARIA classification varies according to the study population and the clinical setting where the study was conducted.

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References

- Grossman J. One airway, one disease. *Chest*. 1997;111:S11-6.
- Bousquet J, Van Cauwenberge P, Khaltaev N; Aria Workshop Group; World Health Organization. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol*. 2001;108:S147-334.
- Bousquet J, Vignola AM, Demoly P. Links between rhinitis and asthma. *Allergy*. 2003;58:691-706.
- Casale TB, Amin BV. Allergic rhinitis/asthma interrelationships. *Clin Rev Allergy Immunol*. 2001;21:27-49.
- Togias A. Unique mechanistic features of allergic rhinitis. *J Allergy Clin Immunol*. 2000;105:S559-604.
- von Mutius E. The rising trends in asthma and allergic disease. *Clin Exp Allergy*. 1998;28 Suppl 5:45-9.
- Nathan RA, Meltzer EO, Selner JC, Storms W. Prevalence of allergic rhinitis in the United States. *J Allergy Clin Immunol*. 1997;99:S808-14.
- Leynaert B, Neukirch F, Demoly P, Bousquet J. Epidemiologic evidence for asthma and rhinitis comorbidity. *J Allergy Clin Immunol*. 2000;106:S201-5.
- Simons FE. Allergic rhinobronchitis: The asthma-allergic rhinitis link. *J Allergy Clin Immunol*. 1999;104:534-40.
- Sibbald B, Rink E. Epidemiology of seasonal and perennial rhinitis: Clinical presentation and medical history. *Thorax*. 1991;46:895-901.
- Guerra S, Sherrill D, Martinez F, Barbee R. Rhinitis as an independent risk factor for adult-onset asthma. *J Allergy Clin Immunol*. 2002;109:419-25.
- Settipane RJ, Hagy GW, Settipane GA. Long-term risk factors for developing asthma and allergic rhinitis: a 23-year follow-up study of college students. *Allergy Proc*. 1994;15:21-5.
- Workshop Report, Global Strategy for Asthma Management and Prevention (GINA). Revised 2002. Initiative World Health Organization, WHO.
- Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report of Working Party on Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J Suppl* 993;16:5-40.
- Bousquet J, Vignola AM, Demoly P. Links between rhinitis and asthma. *Allergy*. 2003;58:691-706.
- Annesi-Maesano I. Epidemiological evidence of the occurrence of rhinitis and sinusitis in asthmatics. *Allergy*. 1999;54(Suppl 57):7-13.
- Marogna M, Falgiani P, Bruno M, Massolo A, Riva G. The allergic march in pollinosis: Natural history and therapeutic implications. *Int Arch Allergy Immunol*. 2004;135:336-42.
- Pereira C, Valero A, Loureiro C, Davila I, Martinez-Cocera C, Murio C, Rico P, Palomino R. Iberian study of aeroallergens sensitisation in allergic rhinitis. *Allerg Immunol*. 2006;38:186-94.

19. Bugiani M, Carosso A, Migliore E, Piccioni P, Corsico A, Olivieri M, Ferrari M, Pirrina P, de Marco R; ISAYA (ECRHS Italy) Study Group. Allergic rhinitis and asthma comorbidity in a survey of young adults in Italy. *Allergy*. 2005;60:165-70.
20. Cirillo I, Vizzaccaro A, Tosca MA, Milanese M, Ciprandi G. Prevalence and treatment of allergic rhinitis in Italian conscripts. *Allerg Immunol (Paris)*. 2003;35:204-7.
21. Annesi-Maesano I, Beyer A, Marmouz F, Mathelier-Fusade P, Vervloet D, Bauchau V. Concurrent allergic diseases: a cross-sectional study in a French population. *Allergy*. 2006;61:390-1.
22. Kapsali T, Horowitz E, Diemer F, Togias A. Rhinitis is ubiquitous in allergic asthmatics. *J Allergy Clin Immunol*. 1997;99:S138.
23. Matsuno O, Miyazaki E, Takenaka R, Ando M, Ito T, Sawabe T, Shigenaga T, Ito K, Sugisaki K, Kumamoto T. Links between bronchial asthma and allergic rhinitis in the Oita Prefecture, Japan. *J Asthma*. 2006;43:165-7.
24. Busse W. Epidemiology of rhinitis and asthma. *Eur Respir Rev*. 1997;7:284-5.
25. Greisner WA, Settipane RJ, Settipane GA. Co-existence of asthma and allergic rhinitis: a 23-year follow-up study of college students. *Allergy Asthma Proc*. 1998;19:185-8.
26. Nihlén U, Greiff L, Montnémy P, Löfdahl CG, Johannisson A, Pearsson C, Andersson M. Incidence and remission of self-reported allergic rhinitis symptoms in adults. *Allergy*. 2006;61:1299-304.
27. Broder I, Higgins MW, Mathews KP, Keller JB. Epidemiology of asthma and allergic rhinitis in a total community. Tecumseh, Michigan IV. Natural history. *J Allergy Clin Immunol*. 1974;54:100-10.
28. Huurre TM, Aro HM, Jaakkola JJ. Incidence and prevalence of asthma and allergic rhinitis: a cohort study of Finnish adolescents. *J Asthma*. 2004;41:311-7.
29. Togias A. Rhinitis and asthma: evidence for respiratory system integration. *J Allergy Clin Immunol*. 2003;111:1171-83.
30. Olaguibel Rivera JM, Alvarez-Puebla MJ, Puy Uribe San Martín M, Tallens Armand ML. Duration of asthma and lung function in life-long nonsmoking adults. *J Investig Allergol Clin Immunol*. 2007;17:236-41.
31. Hellgren J, Toren K, Balder B, Palmqvist M, Lowhagen O, Karlsson G. Increased nasal mucosa swelling in subjects with asthma. *Clin Exp Allergy*. 2002;32:64-9.
32. Linneberg A, Henrik Nielsen N, Frolund L, Madsen F, Dirksen A, Jorgensen T. Copenhagen Allergy Study. The link between allergic rhinitis and allergic asthma: a prospective population-based study. The Copenhagen Allergy Study. *Allergy*. 2002;57:1048-52.
33. Leynaert B, Bousquet J, Neukirch C, Liard R, Neukirch F. Perennial rhinitis: an independent risk factor for asthma in nonatopic subjects. Results from the European Community Respiratory Health Survey. *J Allergy Clin Immunol*. 1999;104:301-4.
34. Boulet LP, Turcotte H, Laprise C, Lavertu C, Bedard PM, Lavoie A, Hebert J. Comparative degree and type of sensitization to common indoor and outdoor allergens in subjects with allergic rhinitis and/or asthma. *Clin Exp Allergy*. 1997;27:52-9.
35. Demoly P, Allaert FA, Lecasble M, Bousquet J; PRAGMA. Validation of the classification of ARIA (Allergic Rhinitis and Its Impact on Asthma). *Allergy*. 2003;58:672-5.
36. Bachert C, van Cauwenberge P, Olbrecht J, van Schoor J. Prevalence, classification and perception of allergic and nonallergic rhinitis in Belgium. *Allergy*. 2006;61:693-8.
37. Bousquet J, Neukirch F, Bousquet PJ, Gehano P, Klossek JM, Le Gal M, Allaf B. Severity and impairment of allergic rhinitis in patients consulting in primary care. *J Allergy Clin Immunol*. 2006;117:158-62.

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