

Interrelationship Between Skin Sensitization, Rhinitis, and Asthma in Patients With Allergic Rhinitis: A Study of Spain and Portugal

A Valero,^{1,2} C Pereira,³ C Loureiro,⁴ C Martínez-Cócerca,⁵ C Murio,⁶ P Rico,⁷ R Palomino,⁸ I Dávila⁹

¹ Allergy Unit, Pneumology and Respiratory Allergy Department, ICT Hospital Clinic, Universitat de Barcelona, Spain (Spanish Study Coordinator)

² Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Spain

³ Immunoallergy Department, Coimbra University Hospital, Coimbra, Portugal, (President of Iberian Chapter of the Sociedad Latinoamericana de Alergia, Asma e Inmunología [SLAAI]).

⁴ Immunoallergy Department, Coimbra University Hospital, Coimbra, Portugal (Portuguese Study Coordinator)

⁵ Allergy Department, Hospital Clínico Universitario de Madrid, Spain (Vice-President of SLAAI)

⁶ Almirall Prodesfarma, Barcelona, Spain

⁷ Medical Department, ALK-Abelló, S.A Madrid, Spain

⁸ Gestió Organització Comunicació S.A (GOC), Barcelona, Spain

⁹ Allergy Department, Hospital Clínico Universitario de Salamanca, Spain (Iberian Chapter of SLAAI)

■ Abstract

Objective: Allergic rhinitis can determine the presence and type of asthma. The main aim of this study was to evaluate the link between allergic rhinitis, asthma, and skin test sensitization in patients with allergic rhinitis.

Methods: Patients with allergic rhinitis, aged 10 to 50 years, were consecutively enrolled at different allergy centers in Spain and Portugal. All the patients underwent skin prick tests with a panel of 20 biologically standardized aeroallergens. Allergic rhinitis was classified according to etiology and the Allergic Rhinitis and its Impact on Asthma guidelines and asthma was classified according to the Global Initiative for Asthma guidelines.

Results: A total of 3225 patients, with a mean age of 27 years, were evaluated. House dust mites and grass and olive tree pollens were the most common aeroallergens. The mean (SD) number of positive skin tests per patient was 6.5 (4), the mean wheal size was 42.3 (28) mm², and the mean atopy index was 6.5 (2). Forty-nine percent of the patients had concomitant asthma. Asthma severity was associated with a longer time since onset ($P < .04$) and allergic rhinitis severity ($P < .001$). Patients with concomitant asthma had a significantly higher number of aeroallergens and sensitization intensity than those without asthma ($P < .001$).

Conclusions: In this broad population sample, the presence and type of asthma was influenced by skin sensitization and both time since onset and severity of allergic rhinitis.

Key words: Aeroallergen sensitization. Rhinitis and asthma comorbidity. Skin prick test.

■ Resumen

Objetivo: Las características de la rinitis pueden condicionar la presencia y el tipo de asma. El objetivo principal de este estudio ha sido evaluar la asociación entre la rinitis, el asma y la sensibilización cutánea a aeroalérgenos en sujetos con rinitis alérgica.

Metodología: Estudio multicéntrico e internacional, realizado en centros de alergia de España y Portugal. Sujetos con rinitis alérgica (entre 10 y 50 años), seleccionados consecutivamente. Se realizaron a todos ellos pruebas cutáneas (prick-test) frente a 20 aeroalérgenos estandarizados biológicamente (ALK-Abelló, S.A., Madrid, Spain). Se clasificó la rinitis alérgica según la guía ARIA, y el asma según GINA.

Resultados: Se estudiaron 3225 sujetos (edad media 27 a.). Los ácaros mayores y los pólenes de gramíneas y olivo fueron los alérgenos más prevalentes. La media de número de sensibilizaciones cutáneas fue de 6,54, la intensidad de sensibilización de 42,328, y el índice de atopia de 6,52. El 49% de los casos tenían asma concomitante. A mayor tiempo de evolución ($P < 0,04$) y gravedad ($P < 0,001$) de la rinitis mayor gravedad del asma. Los sujetos con asma estaban sensibilizados significativamente ($P < 0,001$) a un mayor número de sensibilizaciones y de forma más intensa.

Conclusiones: En nuestra población estudiada, las características de la sensibilización cutánea, el tiempo de evolución y la gravedad de la rinitis alérgica condicionan la presencia y del tipo de asma.

Palabras clave: Sensibilización a aeroalérgenos. Comorbilidad entre rinitis y asma. Pruebas cutáneas.

Introduction

Allergic rhinitis affects between 10% and 25% of the population and recent studies have reported prevalence rates of 26% and 23% in Portuguese and Spanish adults, respectively [1-4]. Several studies have evaluated skin test sensitization to aeroallergens in different populations [5,6].

The Allergic Rhinitis and its Impact on Asthma (ARIA) position paper classifies allergic rhinitis as intermittent or persistent according to its duration, and as mild or moderate to severe according to its severity [1]. The Global Initiative for Asthma (GINA), in turn, classifies asthma as intermittent or persistent according to its duration, and as mild, moderate, or severe according to clinical and lung function criteria [7].

Rhinitis and asthma are common allergic diseases, and epidemiological studies have clearly demonstrated that they are frequently associated [8]. The prevalence of allergic rhinitis is at least 3 times that of asthma [9]. Several studies have reported that allergic rhinitis is an important risk factor for the development of asthma [10,11] and asthma, in turn, has been found to affect between 20% and 70% of patients with allergic rhinitis [11-13].

Allergic rhinitis and asthma profiles are often conditioned by the sensitizing allergen and furthermore, the characteristics of allergic rhinitis may also determine the presence and/or pattern of asthma [11-15].

The aim of this study was to evaluate the interrelationships between allergic rhinitis, asthma, and skin sensitization to a common, biologically standardized panel of aeroallergens in patients with allergic rhinitis.

Methods

We conducted a descriptive, observational, cross-sectional, population-based study in Portugal and Spain.

Subjects

We enrolled patients aged between 10 and 50 years with a diagnosis of allergic rhinitis confirmed by an allergy specialist on the basis of clinical criteria and a positive skin prick test to at least 1 aeroallergen. The patients were recruited from 46 centres in Spain and 18 in Portugal. Written informed consent

was obtained from all participants and the study was approved by ethics and scientific committees in the 2 countries.

Study Design

The study was conducted between October 2004 and March 2005. Each participating center consecutively enrolled patients with allergic rhinitis and administered a questionnaire designed to gather information on sociodemographic characteristics and the diagnosis of both allergic rhinitis (onset and severity without treatment according to ARIA classification [1]) and asthma (according to GINA criteria [7]). All the patients also underwent pulmonary function tests for asthma diagnosis as per GINA guidelines (presence of concomitant disease, onset, severity) and skin prick tests.

Skin Prick Tests

Twenty aeroallergens (ALK-Abelló, S.A, Madrid, Spain), all standardized using biological units and representing the most relevant inhalant allergens in rhinitis and asthma according to previous reports from Portugal and Spain [7], were selected for this study.

The sum of the diameters of all positive skin test reactions was termed sensitization index and the ratio between this index and the number of sensitizations was termed atopy index.

Data Analysis

For the descriptive analysis, continuous variables were described by the mean (SD) and interquartile range (IQR), and categorical variables by the number and percentage of patients in each response category. For bivariate analysis, the χ^2 test was used to compare qualitative variables and the t test to compare both qualitative and quantitative variables. The Kolmogorov-Smirnov test was used to confirm normal distribution and statistical significance was set at $P < .05$ for all statistical tests. Analyses were performed using SPSS version 14.0 (SPSS Inc., Chicago, Illinois, USA).

Results

A total of 3225 patients were correctly studied. The mean age of the sample was 27 years (range, 10-50 y) and 53% of the patients were male.

Characteristics of Skin Sensitization

The most prevalent aeroallergens detected were house dust mites from the *Dermatophagoides* species (63%) and grass (53%). The mean (SD) sensitization index for the sample as a whole was 42 (28) (IQR, 22-57) and the corresponding atopy index was 6.5 (2) (IQR, 5-8). There was a significant correlation ($r=0.88$, $P<.001$) between the number of sensitizations and the sensitization index.

Characteristics of Rhinitis

The mean time since onset for allergic rhinitis was 7 (7) years and the mean (SD) age of onset of rhinitis symptoms was 20 (11) years. According to the ARIA classification system [1], disease was intermittent in 36% of the sample and mild in 59%.

There were no differences between: *a*) time since onset and duration of allergic rhinitis (intermittent vs persistent); *b*) rhinitis severity (mild vs moderate to severe) and number of symptoms in patients with moderate to severe allergic rhinitis; or *c*) number of sensitizations, sensitization index, and atopic index (skin sensitization profile).

Characteristics of Asthma

Asthma, with a mean time since onset of 6.2 (6.0) years, was observed in 49% of patients with allergic rhinitis. The time since onset of rhinitis was significantly higher in patients with asthma (7.9 [7.2] y) than in those without (6.2 [6.3] y) ($P<.001$).

According to the GINA criteria [7], asthma was intermittent in 56% of the group, mild persistent in 33%, moderate persistent in 10%, and severe persistent in just 1%. On analyzing time since onset of asthma, we found that it was 6 (6) years for intermittent disease, 6.4 (6.4) years for mild persistent disease, 7 (5.9) years for moderate persistent disease, and 8.3 (7.0) years for severe persistent disease ($P<.06$, not significant). The corresponding times for allergic rhinitis were 7.6 (6) years for intermittent disease, 8.2 (8) years for mild persistent disease, 9 (9) years for moderate persistent disease, and 12 (9) years for severe persistent disease ($P<.04$).

The age distribution for the onset of allergic rhinitis and asthma is shown in Table 1. In 47% of cases, allergic rhinitis preceded asthma; in 46% of cases, the diseases occurred simultaneously; and in 7% of cases, asthma preceded allergic rhinitis.

Persistent allergic rhinitis and more severe forms of asthma were significantly more frequent in patients with both diseases ($P<.001$) (Table 2), and asthma was more frequent in patients sensitized to house dust mites than in the rest of the patients ($P<.001$).

There were statistically significant differences ($P<.001$) between the number of sensitizations and the presence (7.2 [4]) or absence (5.8 [4]) of asthma and also between the sensitization index and the presence (47.4 [29]) or absence (37.5 [26]) of asthma. Age distribution in relation to sensitization profile and presence of asthma is shown in Table 3.

Table 1. Prevalence and Age of Onset^a of Allergic Rhinitis and Asthma in Patients with Both Diseases

	Patients Aged 10-20 Years	Patients Aged 21-30 Years	Patients Aged 31-40 Years	Patients Aged 41-50 Years
Rhinitis before asthma, % of group	39	49	51	55
Age of onset of rhinitis, y	8.6 (8.8)	16.9 (6.0)	23.4 (11.0)	33.6 (8.1)
Age of onset of asthma, y	12.6 (3.5) ^b	21.3 (4.9) ^b	29.8 (6.0) ^b	39.6 (5.7) ^b
Asthma before rhinitis, % of group	12	6	4	4
Age of onset of rhinitis, y	11.0 (3.9)	19.6 (5.6)	28.5 (4.5)	38.2 (11.3)
Age of onset of asthma, y	6.5 (5.2) ^b	13.0 (8.6) ^b	20.4 (8.2) ^b	28.1 (18.4) ^b
Rhinitis and asthma simultaneously, % of group	49	45	45	41
Age of onset of rhinitis and asthma, y	9.35 (4.2)	17.5 (6.7)	26.2 (8.3)	34.81 (9.0)

^a Presented as mean (SD).

^b $P<.001$ (rhinitis vs asthma).

Table 2. Percentage of Patients With Different Types of Asthma^a According to Type of Allergic Rhinitis^b in Patients With Both Allergic Rhinitis and Asthma

	Intermittent Asthma	Mild Persistent Asthma	Moderate Persistent Asthma	Severe Persistent Asthma
Intermittent allergic rhinitis ^c	42%	23%	20%	24%
Persistent allergic rhinitis	58%	77%	80%	76%
Mild allergic rhinitis ^c	66%	46%	48%	47%
Moderate to severe allergic rhinitis	34%	54%	52%	53%

^a Classified according to the Global Initiative for Asthma guidelines [7].

^b Classified according to the Allergic Rhinitis and its Impact on Asthma Guidelines [1].

^c $P < .001$ (intermittent vs persistent and mild vs moderate to severe).

Table 3. Sex, Skin Sensitization Characteristics, and Prevalence of Asthma for the Population by Age Ranges

Age Range, y	No. of Patients	Skin Sensitization Profile					No. (%) of Patients With Asthma
		Male Patients, %	No of Sensitizations ^a	Sensitization Index ^{a,b}	Atopy Index ^{a,c}		
10-20	1005	61	6.6 (3.3) (4-9)	43.6 (26.0) (24-58)	6.6 (2.0) (5-8)	566 (56.3)	
21-30	1084	41	6.6 (3.7) (4-9)	43.6 (29.0) (23-58)	6.5 (2.0) (5-8)	502 (46.3)	
31-40	745	41	6.3 (3.8) (3-9)	41.4 (29.1) (24-57)	6.5 (2.0) (5-8)	333 (44.7)	
41-50	391	36	5.9 (4.0) (3-9)	37.3 (28.3) (17-51)	6.3 (2.1) (5-7)	180 (46.0)	
<i>P</i>		.001	.001	.001	.2	.001	

^a Data are expressed as means (SD) and interquartile range.

^b Sum of diameters of positive skin test reactions.

^c Ratio between sensitization index and number of sensitizations.

Discussion

The findings of this international multicenter study demonstrate the interrelationship between allergic rhinitis and asthma. The longer the time since onset of allergic rhinitis, the greater both the prevalence and severity of asthma. The sensitization index (sum of diameters of positive skin test reactions) was also higher in patients with asthma and allergic rhinitis than in those with allergic rhinitis only.

We also found that allergic rhinitis characteristics significantly influence the presence and severity of asthma. Several studies have demonstrated that patients with perennial allergic rhinitis have an increased risk of developing asthma. This risk, for example, is increased by 6.7% in subjects with

allergic rhinitis to pollen and by 11.9% in patients allergic to animals (mites, cockroaches and epithelia) [15]. In our study, asthma was more common in mite-sensitized patients than in the rest of the sample.

The severity of allergic rhinitis also influences the development of asthma. The importance of allergic rhinitis in the future development of asthma has been confirmed [13] and patients with persistent allergic rhinitis and severe symptoms have been found to have a 5-fold increased risk of developing asthma [12].

In our study, 47% of patients developed allergic rhinitis, 7% developed asthma first, and 46% developed both diseases

simultaneously. Several studies have reported that allergic rhinitis is typically the first manifestation of an allergic respiratory disease, and in 1 study involving 738 students, allergic rhinitis developed before or at the same time as asthma in 66% and 69% of patients with seasonal and perennial asthma, respectively [16].

Few epidemiological studies have used the same biologically standardized aeroallergen panel as that used in our study. By using a standardized panel, we were able to establish a sensitization profile (sensitization index and atopy index) that can be compared to profiles analyzed in other studies [5, 17-20]. We found polysensitization to be very common in our population, coinciding with reports by other studies [19,21,22].

When analyzing the links between skin sensitization and both asthma and allergic rhinitis, it should be borne in mind that the number and intensity of skin sensitizations are higher in patients with asthma and that atopy indices are higher in those with longer-existing allergic rhinitis [23-25]. Some authors, however, have not found any differences between patients with rhinitis and asthma in terms of number of sensitizations or wheal diameter [19].

In conclusion, we found an interrelationship between allergic rhinitis and asthma and a clear relationship between both these diseases and the characteristics of skin sensitization. Our results support the notion that respiratory allergic disease is a systemic disease and that allergic rhinitis and asthma are manifestations of the same disease. We also found that the characteristics of rhinitis can influence the development and type of asthma.

Researchers

Portugal. North: Graça Castel Branco, Josefina Cernadas, Carmen Botelho, Helena Falcão, Leonor Cunha, Daniela Malheiro, Paula Alendouro, Eliza Mariño, Arminda Guilherme, José Ferreira, Isabel Rosmaninho. **Center:** Celso Chieira, Ana Todo Bom, Graça Loureiro, Emília Faria, Luísa Gerales, Alexandra Santos, Celso Pereira, Carlos Loureiro, Ana Moreti, Miguel Capão Filipe, Isabel Carrapatoso. **South:** Paula Leiria Pinto, Sara Prates, Manuel Barbosa, Elisa Pedro, Manuel Branco Ferreira, Amélia Spínola, Mário Morais Almeida, Elza Tomás, Cristina Arede, Filipe Inácio, Vinhas Sousa, Irina Didenko, Luísa Lopes, Graça Sampaio, Felicidade Dias, Carlos Nunes, Susel Ladeira, Beatriz Tavares, Rita Câmara, Susana Oliveira.

Spain. Mediterranean area: Albert Roger Reig-Coordinator, Alex Roger Reig, Alfonso Olivé Pérez, Ángel Julio Huertas Amorós, Antonio Valero Santiago, César Alias Tuduri, Javier Montoro Lacomba, José María Negro Álvarez, José Ramón Lavín Alonso, Josep Maria Roger Barri, Juan Antonio Pagán Alemán, Lluís Marqués Amat, M^a Dolores Martos Clahorro, M^a Teresa Dordal i Culla, Mercè Corominas Sánchez, Miguel Ángel Baltasar Drago, Miguel Ángel Díaz Palacios, Pol Pau, Ramon Leonart Bellfill, Ramon Serra Juanpere, Rosa M^a Martínez López, Santiago Aparicio Español, Silvia Lara Alcón, Teresa Abós Mir. **South:** Julio Delgado Romero- Coordinator, Alfonso Del Cuvillo Bernal, Ana María Navarro Pulido, Carmen Moreno Escobosa, Dr. Porcel Carreño, Dra. Alvarado Arenas, Dr. Jiménez Timón,

Esperanza Sanz Romero, Francisco Burgos Gómez, Francisco Javier Hernández Arbeiza, Francisco Moreno Benítez, Jesús Miguel García Menaya, José Amat López, José Carlos Orta Cuevas, José Luis Justicia Ruano, Laureano Fernández-Távora Fernández, M. Angeles Gonzalo Garijo, M^a Angeles Lara Jiménez, M^a Carmen Moya Quesada, M^a Cesárea Sánchez Hernández, M^a Sergia Cruz Granados, Remedios Pérez Calderón, Susana Duran Macarro. **Canary Islands:** Inmaculada Sánchez Machín- Coordinator, Juan Antonio García Marrero, Ruperto González Pérez, Anselmo Sánchez Palacios, Fernando de la Torre Morín, Fernando Schamann Medina, Javier Figueroa Ribero, José Carlos Robaina, Paloma Poza Guedes; **North:** Eduardo Fernández Ibáñez- Coordinator, Alejandro Joral Badas, Alicia Suárez Rodríguez, Beatriz Valeiro Pérez, Elena Ordoqui, Encarnación Antón Casas, Eulalia Camino Rodríguez, Gonzalo Bernaola Hortigüela, Isabel Jiménez Gómez, José Antonio Navarro, José Carlos García Ortiz, José Fernando Filgueira Iglesias, José Francisco Garmendia, Juan Jerez Domínguez, María Teresa Soto Mera, Marta Orta, Noemí Saiz Cordero, Sofía Alonso Juaristi, Teófilo Lobera. **Center:** Javier Domínguez Ortega- Coordinator, Alicia Alonso Gómez, Ana Alonso Llamazares, Ana Rosado Ingelmo, Angel Moral de Gregorio, Belén Añibarro, Carlos Senent Sánchez, Carmen Panizo Gravo, Concepción Vila Albelda, Consuelo Martínez Cócera, Elena Laffond Yges, Eloína González Mancebo, Esther Moreno Rodilla, Ignacio Dávila González, M^a Dolores Herrero Gil, M^a Luisa González Gutiérrez, María del Mar Moro Moro, María Isabel Esteban, María Teresa Gracia Bara, Marta Chamorro, Marta López San Martín, Mercedes Martínez San Ireneo, Miguel Ángel Tejedor Alonso, Nieves Cabañes Higuero, Rosa M^a Blanco González, Sara Acero Sainz, Tomás Chivato.

Acknowledgments

This study was promoted by the Iberian Chapter of the Sociedad Latinoamericana de Alergia, Asma e Inmunología (SLAAI), which brings together the Portuguese and Spanish allergy and clinical immunology societies (Sociedad Portuguesa de Alergia e Inmunología Clínica [SPAIC] and Sociedad Española de Alergia e Inmunología Clínica [SEAIC]). Despite the logistic and financial support provided by the sponsors of the study (Allmiral Prodesfarma and ALK-Abelló), the scientific committee had full freedom to conduct the project.

We thank Dr Joan Heras from Almirall Prodesfarma Spain, Dr Santiago Martin Hurtado from ALK-Abelló Spain, and Professor Carlos Crisci, President of SLAAI.

References

1. Bousquet J, van Cauwemberge P, Khaltaev N. ARIA Workshop Group. World Health Organization. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001; 108 (suppl 5): S147-S334.
2. Ciprandi G, Vizzaccaro A, Cirrillo I, Crimi P, Canonica GW. Increase of asthma and allergic rhinitis prevalence in young Italian men. *Int Arch Allergy Immunol* 1996; 111: 278-83.

3. Arnedo-Pena A, Garcia Marcos L, Hernandez G. Time trends and geographical variations in the prevalence of symptoms of allergic rhinitis in 6-7-year-old children from eight areas of Spain according to the ISAAC. *An Pediatr (Barc)*. 2005; 62(3): 229-36.
 4. Bauchau V, Durham SR. Prevalence and rate of diagnosis of allergic rhinitis in Europe. *Eur Respir J* 2004; 24:758-64.
 5. Heinzerling L, Frew AJ, Bindslev-Jensen C, Bonini S, Bousquet J, Bresciani M, Carlsen KH, van Cauwenberge P, Darsow U, Fokkens WJ, Haahtela T, van Hoecke H, Jessberger B, Kowalski ML, Kopp T, Lahoz CN, Lodrup Carlsen KC, Papadopoulos NG, Ring J, Schmid-Grendelmeier P, Vignola AM, Wöhrl S, Zuberbier T. Standard skin prick testing and sensitisation to inhalant allergens across Europe – a survey from the GA2LEN network. *Allergy* 2005; 60:1287-300.
 6. Pereira C, Valero A, Loureiro C, Davila I, Martinez-Cocera, Murio C, Rico P, Palomino R. Iberian study of aeroallergens sensitisation in allergic rhinitis. *Allerg Immunol* 2006; 38: 186-94.
 7. Workshop Report, Global Strategy for Asthma Management and Prevention (GINA). Initiative World Health Organization, WHO. Updated October 2005. <http://www.ginasthma.com/>.
 8. Leynaert B, Neukirch F, Demoly P, Bousquet J. Epidemiologic evidence for asthma and rhinitis comorbidity. *J Allergy Clin Immunol* 2000; 106: 201–5.
 9. Togias A. Rhinitis and asthma: evidence for respiratory system integration. *J Allergy Clin Immunol* 2003; 111: 1171-83.
 10. 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.
 11. Guerra S, Sherrill DL, Martinez FD, Barbee RA. Rhinitis as an independent risk factor for adult-onset asthma. *J Allergy Clin Immunol* 2002; 109: 419-25.
 12. Leynaert B, Neukirch F, Demoly P, Bousquet J. Epidemiologic evidence for asthma and rhinitis comorbidity. *J Allergy Clin Immunol* 2000; 106 (suppl 5): S201-205.
 13. Marogna M, Fallagani 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.
 14. Cirillo I, Vizzacaro A, Tosca MA, Milanese M, Ciprandi G. Prevalence and treatment of allergic rhinitis in Italian conscript subjects. *Eur Ann allergy Clin Immunol* 2003; 35: 204-7.
 15. Leynaert B, Bousquet J, Neukirch C, Liard R, Neukirch CF. Perennial rhinitis: an independent risk factor for asthma in non-atopic subjects. Results from the European Community Respiratory Health Survey. *J Allergy Clin Immunol* 1999; 104: 301-4.
 16. Huse DM, Hartz SE, Russell MW, Piercey G, Weiss ST. Allergic rhinitis may worsen asthma symptoms in children: the international asthma outcomes registry (abstract). *Am J Respir Crit Care Med* 1996; 153: A860.
 17. Hader S, Kuhr J, Urbanek R. sensitisation to 10 important air-borne allergens in school children. *Monatsschr kinderheilkd* 1990; 138: 66-71.
 18. Eriksson NE, Holmen A. Skin prick tests with standardized inhalant allergens in 7099 adult patient with asthma or rhinitis: cross-sensitisations and relationships to age, sex, month of birth and year testing. *J Investig Allergol Clin Immunol* 1996; 6: 36-46.
 19. Montealegre F, Meyer B, Chardon D, Vargas W, Zavala D, Hart B, Bayona M. Comparative prevalence of sensitisation to common animal, pollen and mould allergens in subjects with asthma, or atopic dermatitis and/or allergic rhinitis living in a tropical environment. *Clin Exp Allergy* 2004; 34: 51-8.
 20. Verini M, Rossi N, Verrotti A, Pelaccia G, Nicodemo A, Chiarelli F. Sensitisation to environmental antigens in asthmatic children from a central Italian area. *Sci total environ* 2001; 270: 63-9.
 21. Bozkurt B, Karakaya G, Kalyoncu AF. Seasonal rhinitis, clinical characteristics and risk factors for asthma. *Int Arch allergy Immunol* 2005; 138: 73-9.
 22. Celedon J, Palmer L, Weiss S, Wang B, Fang Z, Xu X. Asthma, rhinitis, and skin test reactivity to aeroallergens I families of asthmatics subjects in Anqing, China. *Am J Respir Crit Care Med* 2001; 163; 1108-12.
 23. Baratawidjaja IR, Baratawidjaja PP, Darwis A, Soohwee L, Fook-Tim C, Bee-Wah L, Baratawidjaja KG. Prevalence of allergic sensitisation to regional inhalants among allergic patients in Jakarta, Indonesia. *Asian Pac J Allergy Immunol*, 1999; 17: 9-12.
 24. Sears MR, Herbison GP, Holdaway MD, Hewit CJ, Flannery EM, Silva PA. The relative risk of sensitivity to grass pollen, house dust mite, cat dander in the development of childhood asthma. *Clin Exp Allergy* 1989; 19: 419-24.
 25. Sears MR, Burrows B, Flannery EM, Herbison GP, Holdaway MD. Atopy in childhood. Gender and allergen related risks for development of hay fever and asthma. *Clin Exp Allergy* 1993; 23: 883-5.
- *Manuscript received September 5, 2008; accepted for publication, October 6, 2008.*
- **Antonio Luis Valero Santiago**
- Unidad de Alergia, Servicio de Neumología y Alergia Respiratoria.
ICT, Hospital Clinic i Universitari de Barcelona.
C/ Villarroel 170, 08036 Barcelona, Spain
E-mail: valero@clinic.ub.es