Allergic rhinitis and associated factors in schoolchildren from Bogotá, Colombia*

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Rhinology 50: 122-128, 2012 **DOI:**10.4193/Rhino11.175

*Received for publication:

August 11, 2011

Accepted: December 21, 2011

Summary

Background: Allergic rhinitis is one of the most frequent chronic diseases among children. The objective of the study was to assess the prevalence of and the factors associated with self-reported allergic rhinitis symptoms in schoolchildren from Bogotá, Colombia.

Methodology: We followed the International Study of Asthma and Allergies in Childhood (ISAAC) methodology. Our sample included 3,256 children aged 6 - 7 and 3,830 adolescents aged 13 - 14 years.

Results: The prevalence of self-reported allergic rhinitis symptoms was 30.8% among children and 36.6% among adolescents. Factors associated with self-reported allergic rhinitis among children included current asthma and atopic dermatitis symptoms; use of acetaminophen in the first year of life and in the last 12 months; antibiotic use in the first year of life; high-school and university maternal education; smokers at home; and caesarean delivery. Among adolescents, associated factors included current asthma and atopic dermatitis symptoms; current acetaminophen use once per month; frequent fast-food consumption; cat exposure at home; and smoking.

Conclusions: Further exploration of factors associated with allergic rhinitis symptoms is needed.

Key words: allergic rhinitis, prevalence, associated factors, ISAAC-III, Bogotá, Colombia

Introduction

Allergic rhinitis is one of the most frequent chronic diseases among children. Its prevalence varies across different geographical zones and even within the same country. Allergic rhinitis has been frequently associated with different respiratory tract pathologies such as asthma, sinusitis or otitis, which are main causes of primary attention worldwide. In addition to the high

economic impact of this pathology, it affects the quality of life of those affected in terms of daily physical activity, attention, sleep habits and social relationships.

Even though allergic rhinitis is a common disease around the world, its epidemiology is just starting to be known. In some countries, the disease is reaching epidemic levels and it is

becoming a public health issue. Different regions of the world report prevalence rates between 10% and 40% (1), but the lack of a standardized diagnosis makes comparisons difficult among different populations. To overcome these limitations, the International Study of Asthma and Allergies in Childhood (ISAAC) was designed as a multicentre-study to investigate the epidemiology of asthma, rhinitis and atopic dermatitis among children using standardized definitions, allowing comparisons worldwide.

Despite the relatively high frequency of allergic rhinitis, there are no studies addressing its prevalence and associated factors among children in Colombia. A previous study conducted in 2004 estimated that the prevalence of allergic rhinitis in the general population was 16% ⁽²⁾. A second report, conducted in the city of Cali in 2003, found that 18% of kindergarten children aged 2-3 years suffered from allergic rhinitis ⁽³⁾. These studies did not take into account socio-demographic, medical and environmental factors, which may participate in the development of the disease, and therefore, may constitute targets for interventions or medical treatment intended to achieve better results.

Therefore, the aim of this study was to assess the prevalence of and the factors associated with allergic rhinitis symptoms among schoolchildren aged 6 - 7 and 13 - 14 years in Bogotá, Colombia, based on the results obtained from the ISAAC phase-III conducted in this region.

Materials and methods

Study design

This cross-sectional study took place in Bogota, the capital city of Colombia, between March and September 2002. Bogotá is located 2,640 meters above sea level, has a subtropical climate with no seasonal changes other than alternate rainy and dry periods, and a population reaching 6,712,247 inhabitants in 2002. From a total of 4,535 registered educational institutions in Bogota in 2002, we randomly selected 74 schools for children aged 6 - 7 years and 48 schools for adolescents aged 13 - 14 years; all of them belonging to middle socio-economic strata ⁽⁴⁾.

All the information was collected following the ISAAC methodology ⁽⁵⁾. Two Spanish language versions of the written questionnaires (WQ) were proposed given the students' age: for the group of children aged 6 - 7 years, parents/tutors were asked to answer the questionnaire; whereas the group of adolescents aged 13 - 14 years were asked to answer the questionnaire by themselves. All schoolchildren within the age-groups of interest were invited to participate in the study without any incentive. The study was approved by the institutional ethics committee of the Fundación Santa Fe de Bogotá.

Variables

The dependent variable of self-reported allergic rhinitis symptoms corresponds to the question: 'In the past 12 months, have you had a problem with sneezing, or a runny, or blocked nose when you DID NOT have a cold or the flu?' from the core rhinitis module of the WQ.

All independent variables were drawn from the environmental questionnaire (6). In brief, they included the use of acetaminophen and antibiotics; the frequency consumption of meat, seafood, fruits, vegetables, pulses, cereals, pasta, rice, butter, margarine, nuts, potatoes, milk, eggs and fast-food; time spent exercising and watching television; exposure to smoking; maternal education; frequency of vehicle traffic near the household; exposure to animals (cats, dogs and farm animals); family size; cooking fuel; breastfeeding; and caesarean delivery. The prevalence rates of self-reported asthma and atopic dermatitis symptoms were drawn from the following two questions: 'Have you had wheezing or whistling in the chest in the last 12 months?' and 'Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?', from to the wheezing and eczema core WQ respectively. Finally, we used the question: 'Have you ever had hay fever?' from the core rhinitis module of the WQ as a surrogate of ever having a diagnosis of hay fever.

Statistical analysis

All analyses were conducted with the software STATA version 8.0. The prevalence rates of self-reported allergic rhinitis, asthma and atopic dermatitis symptoms were calculated together with their 95% confidence intervals. Then, a bivariate analysis was carried out between the dependent and each independent variable separately. Finally, we conducted a multivariable analysis including only those independent variables with a p-value < 0.10 in the bivariate analysis. P-values < 0.05 were considered statistically significant in the multivariable analysis.

Results

The study population included 3,256 children aged 6-7 years (56.2% girls; 43.8% boys), and 3,829 adolescents aged 13 - 14 years (52.7% girls; 47.3% boys). The response rate was 89.5% for the group of children and 98.7% for the group of adolescents.

Prevalence

Results from the WQ are shown in Table 1. The prevalence of self-reported allergic rhinitis symptoms was higher in adolescents (36.6%) than in children (30.8%), p < 0.001. Both in the group of children and in the group of adolescents, the prevalence between boys and girls was not statistically significantly different in either group.

Table 1. Prevalence of allergic symptoms reported in the written questionnaire with a positive answer in schoolchildren from Bogota, Colombia.

Symptoms	Children aged 6-7 yrs (n = 3,256)			Adolescents aged 13-14 yrs (n = 3,829)		
		%	95% CI		%	95% CI
Prevalence of allergic rhinitis in the last 12 months	979	30.8	(29.2-32.4)	1386	36.57	(35.0-38.1)
Presence of allergic rhinitis in the last 12 months in combination with						
Asthma in the last 12 months	206	6.7	(5.8-7.5)	203	5.4	(4.7-6.1)
Atopic dermatitis in the last 12 months	221	7.0	(6.2-8.0)	222	6.0	(5.2-6.7)
Asthma and atopic dermatitis in the last 12 months	51	1.7	(1.2-2.1)	48	1.3	(0.9-1.7)
Hay fever ever	588	18.3	(16.9-19.6)	687	18.11	(16.9-19.3)

95% CI: 95 % confidence interval of the percentage

An important relationship was found between the prevalence of self-reported allergic rhinitis and the other allergic diseases, where up to 7% of children and 6% of adolescents reported allergic rhinitis in combination with atopic dermatitis symptoms in the last 12 months.

Analysis of associated factors

From the set of independent variables, we show only those associated with self-reported allergic rhinitis symptoms reaching a p-value < 0.05 in the multivariable analysis (Tables 2 and 3).

Among children, factors associated with self-reported allergic rhinitis symptoms in the last 12 months in the multivariable analysis included: self-reported asthma and atopic dermatitis symptoms in the last 12 months, acetaminophen use in the first year of life and in the last 12 months, antibiotic use in the first year of life, higher maternal education, more than one smoker at home, and caesarean delivery (Table 2).

Among adolescents, factors associated with self-reported allergic rhinitis symptoms in the last 12 months in the multivariable analysis included: self-reported asthma and atopic dermatitis symptoms in the last 12 months, acetaminophen use in the last 12 months once a year, consumption of fast-food three or more times a week, exposure to cats at home in the last 12 months, and smoking at least once in their lives (Table 3).

Discussion

In this study, the authors used the results from the ISAAC phase-III to estimate the prevalence of allergic rhinitis symptoms and its associated factors among children and adolescents in Bogotá, the biggest settlement of Colombia. These

results may guide public health policies oriented to improve the management of this pathology in the studied region.

We found differences between the studied age-groups. The prevalence of self-reported allergic rhinitis symptoms in the last 12 months appeared to be high, with 30.8% among children and 36.6% among adolescents. The fact that adolescents had a higher prevalence of allergic rhinitis, compared to children, may be due to an actual increase in the prevalence of symptoms during this period of life. Alternatively, adolescents themselves could have a better perception of symptoms than parents answering for their children.

After seven years, results from the ISAAC phase-III show an upward trend in the prevalence of allergic rhinitis symptoms, ranging between 2.2% and 45.1% in the participating centres ⁽⁷⁾. Moreover, the increase was more common in the group of children than in the group of adolescents. Although several study groups have reported a wide variety of results for both age-groups, most of them describe an increase in the prevalence of the three allergic conditions (asthma, allergic rhinitis and atopic dermatitis) ⁽⁸⁻¹²⁾.

Our results show boys and girls do not show a significant difference in prevalence rates of self-reported allergic rhinitis symptoms in the last 12 months. In general, the natural history of the disease shows initially higher prevalence rates among boys during childhood (13), shifting later to be higher among females during adolescence and adulthood (14). However, the German study that compared ISAAC phases I (1995) and III (2000), found that girls had a higher prevalence of allergic rhinitis than boys in both periods, and a tendency to increase

Table 2. Factors associated with self-reported allergic rhinitis symptoms in children aged 6-7 years from Bogotá, Colombia.

Variables	Bivariate analysis			Multivariable analysis			
	OR	95% CI	p-value	OR	95% CI	p-value	
Prevalence of asthma symptoms in the la	st 12 months						
No	1.0			1.0			
Yes	5.0	(3.9-6.4)	< 0.001	3.8	(2.7-5.3)	< 0.001	
Prevalence of atopic dermatitis symptoms in the last 12 months							
No	1.0			1.0			
Yes	2.5	(2.1-3.1)	< 0.001	2.3	(1.7-3.0)	< 0.001	
Use of acetaminophen in the first year of	life						
No	1.0			1.0			
Yes	1.9	(1.6-2.3)	< 0.001	1.5	(1.2-1.9)	0.002	
Use of acetaminophen in the last 12 mor	iths						
No	1.0			1.0			
Once a year	3.1	(2.2-4.5)	< 0.001	2.9	(1.7-4.7)	< 0.001	
Once a month	1.9	(1.3-2.7)	0.001	2.1	(1.3-3.5)	0.004	
Use of antibiotics in the first year of life	1.0			1.0			
No	1.0	(4.5.2.4)	0.004	1.0	(4.4.4.7)	0.043	
Yes	1.8	(1.5-2.1)	< 0.001	1.3	(1.1-1.7)	0.012	
Maternal educational level	1.0			1.0			
Primary school	1.0	(a. a. a. a)		1.0	(4.0.4.0)		
High school	1.3	(1.1-1.6)	0.012	1.4	(1.0-1.9)	0.033	
University	1.5	(1.2-2.0)	0.001	2.1	(1.5-2.9)	< 0.001	
Number of smokers at home							
None	1.0			1.0			
One person	1.1	(0.9-1.4)	0.234	1.1	(0.8-1.4)	0.710	
More than one person	1.2	(1.0-1.5)	0.016	1.3	(1.0-1.7)	0.020	
Caesarean delivery							
No	1.0	(a.a.a.=)		1.0	(4.4.4.7)		
Yes	1.3	(1.1-1.5)	0.007	1.4	(1.1-1.7)	0.005	

95% CI: 95 % confidence interval of the odds ratio

Results are presented for significant variables in the multivariable analysis with $p < 0.05\,$

during the phase-III (10). Similar conclusions were drawn in Spain (15), Estonia (16), Brazil (11), Finland (17), and the United Kingdom (18). In contrast, Taiwan reported a higher prevalence in boys (19).

Results in Bogotá show a positive association with self-reported asthma and atopic dermatitis symptoms in the last 12 months in both age groups. The link among allergic pathologies is in accordance with international reports from the ISAAC and Colombia ⁽⁴⁾. This confirms the close relationship existing among them and supports the concept of allergy as a systemic condition mainly affecting the nasal mucous, the respiratory

tract and the skin.

Another risk factor associated with allergic rhinitis was the use of acetaminophen during the first year of life for children and in the last 12 months for both children and adolescents. This finding is in accordance with other reports showing that acetaminophen use during the first year of life acts as a risk factor for allergic rhinitis and asthma ⁽²⁰⁾. The proposed explanation for the association between acetaminophen use and allergic diseases lies in the ability of acetaminophen to diminish antioxidants and to promote the Th2 response ⁽²¹⁾.

Table 3. Factors associated with self-reported allergic rhinitis symptoms in adolescents aged 13-14 years from Bogotá, Colombia.

Variables	Bivariate analysis			M	Multivariable analysis			
	OR	95% CI	p-value	OR	95% CI	p-value		
Prevalence of asthma in the last 12 months								
No	1.0							
Yes	3.3	(2.6-4.2)	< 0.001	2.9	(2.2-3.8)	< 0.001		
Prevalence of atopic dermatitis in the last 12 months								
No	1.0							
Yes	1.7	(1.4-2.1)	< 0.001	1.5	(1.2-1.9)	< 0.001		
Use of acetaminophen in the last 12 months								
No	1.0							
Once a year	1.0	(0.8-1.3)	0.835	0.9	(0.7-1.2)	0.612		
Once a month	1.7	(1.4-2.0)	< 0.001	1.6	(1.2-2.0)	< 0.001		
Consumption of fast-food								
Never or occasionally	1.0							
Once or twice a week	1.1	(1.0-1.3)	0.153	1.1	(0.9-1.3)	0.378		
Three or more times a week	1.4	(1.1-1.7)	0.005	1.3	(1.0-1.7)	0.021		
5								
Exposure to cats at home in the last 12 months								
No	1.0	(4.0.4.5)	0.075	1.3	(4.0.4.7)	0.007		
Yes	1.2	(1.0-1.5)	0.075	1.3	(1.0-1.7)	0.027		
Smoked ever	1.0							
No	1.0	(4.2.4.7)	0.001		(4.2.4.7)	0.001		
Yes	1.5	(1.3-1.7)	< 0.001	1.4	(1.2-1.7)	< 0.001		

95% CI: 95 % confidence interval of the odds ratio

Results are presented for significant variables in the multivariable analysis with p < 0.05

In the group of adolescents, the consumption of fast-food three or more times a week constituted an associated factor. This finding is in agreement with results from the ecological analysis of dietary habits under the ISAAC, which suggested that western-type diets including margarine, trans-fatty acids, animal fats and fast-foods constituted risk factors; whereas diets based on vegetables, cereals, fruits, seafood, peanuts and olive oil constituted protective factors (22).

In the group of children, high school and university maternal education was positively associated with the presence of allergic rhinitis symptoms in their children. One possible explanation may be that higher education is related to higher socio-economic status, better awareness of symptoms and understanding of questions, and more reliable responses in this group of mothers, in addition to better opportunities for diagnosis and access to medical treatment.

Additionally, we found a positive association with caesarean delivery in the group of children, although the literature covering this finding remains controversial. A prospective study conducted in Norway showed an association between caesarean delivery and food-allergy among susceptible children (23). Other studies conducted in Finland and the United Kingdom showed contradictory results, probably due to heterogeneous measurements (24,25). Finally, a recent meta-analysis found that caesarean delivery was associated with a moderate risk of allergic rhinitis (26). Several studies have shown that the intestinal flora of children born by caesarean section is different from those delivered vaginally, showing a high colonisation of Clostridium difficile and low counts of Bifidobacterium and Lactobacillus in children born by caesarean section, following a western life-style, presenting food-allergies and having positive skin prick test reactions (27). However, differences may be related to mucous-specific factors associated with atopy, as mentioned by one of the authors.

The positive association between smoking at home and allergic rhinitis symptoms in both age groups is in agreement with previous reports worldwide (28). It has been demonstrated that smoking increases the permeability of respiratory mucous membranes, the production of total and cord-blood IgE, and the number of Th2 lymphocytes involved in allergic responses. However, it has not been demonstrated if smoking increases the allergic sensitisation. Finally, children whose parents smoke at home are at an increased risk of developing bronchial asthma; however, this association is still to be demonstrated for allergic rhinitis.

Finally, exposure to domestic animals was positively associated with allergic rhinitis symptoms in both age groups. A similar trend was observed in mothers exposed to domestic animals during pregnancy, although the association was no longer significant in the multivariable analysis. Whether the exposure to cats during infancy is related to subsequent allergic sensitisation or not remains controversial. Some authors hypothesise that having a cat at home will foster allergen exposure, increasing the risk of sensitisation in susceptible children (29). In contrast, other authors suggest that endotoxins are more

abundant in homes with pets, which may protect against allergic sensitisation by the induction of Th1-type immune responses ⁽³⁰⁾.

In conclusion, this study shows a high prevalence of self-reported allergic rhinitis symptoms in children aged 6 - 7 years and adolescents aged 13 - 14 years of middle socio-economic strata in Bogotá, Colombia. We were able to confirm the strong association between allergic rhinitis and other allergic diseases like asthma and atopic dermatitis, as well as with other independent factors like the use of antibiotics and acetaminophen, smoking exposure, dietary habits and the exposure to household pets.

Acknowledgements

The authors would like to thank Martha Delgado and Martin Rondón for their helpful suggestions during the data analysis. This study was supported by GlaxoSmithKline, Astra Zeneca and Boehringer-Ingelheim.

Conflict of interest

The authors declare no conflict of interest.

References

- Bousquet J, Van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol. 2001; 108: S147-S334.
- 2. Dennis R, Caraballo L, Garcia E, et al. Asthma and other allergic conditions in Colombia: a study in 6 cities. Ann Allergy Asthma Immunol. 2004; 93: 568-574.
- Arévalo-Herrera M, Reyes MA, Victoria L, Villegas A, Badiel M. Asthma and allergic rhinitis in pre-school children of Cali [In Spanish]. Colombia Médica. 2003; 34: 4-8.
- Garcia E, Aristizabal G, Vasquez C, Rodriguez-Martinez CE, Sarmiento OL, Satizabal CL. Prevalence of and factors associated with current asthma symptoms in school children aged 6-7 and 13-14 yr old in Bogota, Colombia. Pediatr Allergy Immunol. 2008; 19: 307-314.
- Ellwood P, Asher MI, Beasley R, Clayton TO, Stewart AW. The international study of asthma and allergies in childhood (ISAAC): phase three rationale and methods. Int J Tuberc Lung Dis. 2005; 9: 10-16.
- ISAAC Steering Committee. International Study of Asthma and Allergies in Childhood. Phase Three Manual. Available at: http://isaac.auckland.ac.nz (accessed 3 January 2007).
- Asher MI, Montefort S, Bjorksten B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet. 2006; 368: 733-743.
- 8. Lee SL, Wong W, Lau YL. Increasing prev-

- alence of allergic rhinitis but not asthma among children in Hong Kong from 1995 to 2001 (Phase 3 International Study of Asthma and Allergies in Childhood). Pediatr Allergy Immunol. 2004; 15: 72-78.
- Tamay Z, Akcay A, Ones U, Guler N, Kilic G, Zencir M. Prevalence and risk factors for allergic rhinitis in primary school children. Int J Pediatr Otorhinolaryngol. 2007; 71: 463-471.
- 10. Maziak W, Behrens T, Brasky TM, et al. Are asthma and allergies in children and adolescents increasing? Results from ISAAC phase I and phase III surveys in Munster, Germany. Allergy. 2003; 58: 572-579.
- Borges WG, Burns DA, Felizola ML, Oliveira BA, Hamu CS, Freitas VC. Prevalence of allergic rhinitis among adolescents from Distrito Federal, Brazil: comparison between ISAAC phases I and III. J Pediatr (Rio J). 2006; 82: 137-143.
- Lis G, Breborowicz A, Cichocka-Jarosz E, et al.
 The prevalence of allergic rhinitis and conjunctivitis in school children from Krakow and Poznan--ISAAC study (International Study of Asthma and Allergies in Childhood) [In Polish]. Otolaryngol Pol. 2004; 58: 1103-1109.
- 13. International Rhinitis Management Working Group. Epidemiology of Rhinitis. Allergy. 1994; 49: 19.
- Strachan DP. Epidemiology of rhinitis. In: Busse WW, Holgate ST, eds. Asthma and Rhinitis. Oxford: Blackwell Scientific Publications. 2000; 33-42.
- 15. Tornador-Gaya E, Tosca-Segura R, Arnedo-Pena A, et al. Incidence of allergic rhinitis in

- a cohort of schoolchildren between 1994 and 2002 in Castellon (Spain), following the ISAAC study [In Spanish]. An Pediatr (Barc). 2007; 66: 154-158.
- Annus T, Riikjarv MA, Rahu K, Bjorksten B. Modest increase in seasonal allergic rhinitis and eczema over 8 years among Estonian schoolchildren. Pediatr Allergy Immunol. 2005; 16: 315-320.
- Remes ST, Korppi M, Kajosaari M, Koivikko A, Soininen L, Pekkanen J. Prevalence of allergic rhinitis and atopic dermatitis among children in four regions of Finland. Allergy. 1998; 53: 682-689.
- Shamssain MH, Shamsian N. Prevalence and severity of asthma, rhinitis, and atopic eczema in 13- to 14-year-old schoolchildren from the northeast of England. Ann Allergy Asthma Immunol. 2001; 86: 428-432.
- Liao MF, Huang JL, Chiang LC, Wang FY, Chen CY. Prevalence of asthma, rhinitis, and eczema from ISAAC survey of schoolchildren in Central Taiwan. J Asthma. 2005; 42: 833-837.
- Davey G, Berhane Y, Duncan P, Aref-Adib G, Britton J, Venn A. Use of acetaminophen and the risk of self-reported allergic symptoms and skin sensitization in Butajira, Ethiopia. J Allergy Clin Immunol. 2005; 116: 863-868.
- 21. Shaheen SO, Sterne JA, Songhurst CE, Burney PG. Frequent paracetamol use and asthma in adults. Thorax. 2000; 55: 266-270.
- 22. Ellwood PE, Asher MI, Björkstén B, et al. Diet and Asthma, Allergic Rhinoconjunctivitis and Atopic Eczema symptom prevalence: An ecological analysis of the International Study of Asthma and Allergies in Childhood

- (ISAAC) data. Eur Respir J. 2001; 17: 436-443.
- 23. Eggesbo M, Botten G, Stigum H, Samuelsen SO, Brunekreef B, Magnus P. Cesarean delivery and cow milk allergy/intolerance. Allergy. 2005; 60: 1172-1173.
- 24. Kero J, Gissler M, Gronlund MM, et al. Mode of delivery and asthma is there a connection? Pediatr Res. 2002; 52: 6-11.
- 25. Maitra A, Sherriff A, Strachan D, Henderson J. Mode of delivery is not associated with asthma or atopy in childhood. Clin Exp Allergy. 2004; 34: 1349-1355.
- 26. Bager P, Wohlfahrt J, Westergaard T. Caesarean delivery and risk of atopy and allergic disease: meta-analyses. Clin Exp Allergy. 2008; 38: 634-642.
- 27. Kalliomaki M, Kirjavainen P, Eerola E, Kero P, Salminen S, Isolauri E. Distinct patterns of

- neonatal gut microflora in infants in whom atopy was and was not developing. J Allergy Clin Immunol. 2001; 107: 129-134.
- 28. Mitchell EA, Stewart AW. The ecological relationship of tobacco smoking to the prevalence of symptoms of asthma and other atopic diseases in children: the International Study of Asthma and Allergies in Childhood (ISAAC). Eur J Epidemiol. 2001; 17: 667-673.
- 29. Apelberg BJ, Aoki Y, Jaakkola JJ. Systematic review: Exposure to pets and risk of asthma and asthma-like symptoms. J Allergy Clin Immunol. 2001; 107: 455-460.
- 30. Waser M, von Mutius E, Riedler J, et al. Exposure to pets, and the association with hay fever, asthma, and atopic sensitization in rural children. Allergy. 2005; 60: 177-184.

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