
“Early” cat ownership and the risk of sensitization and allergic rhinitis in Ligurian children with respiratory symptoms

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Background: Studies on the role of cat ownership in the development of allergy have lead to conflicting results, probably owing to heterogeneity of the populations evaluated.

Objective: To evaluate the possible effect of cat ownership on the frequency of sensitization and asthma or rhinitis in children living in Liguria, Italy, who attended a pediatric clinic for respiratory symptoms.

Methods: We enrolled 269 consecutive school-aged children in 12 months. Sensitization to aeroallergens by skin prick testing and the presence of respiratory symptoms (ie, asthma and rhinitis) were evaluated. To analyze the role of different independent variables in association with respiratory symptoms and sensitization, a multiple logistic regression analysis was performed.

Results: Of 269 children, 81 were exposed to cats at home in the first 2 years of life (“early” cat owners), 65 after the first 2 years of life (“late” cat owners), and 123 never (“never” cat owners). Early cat ownership was significantly associated with a lower risk of cat sensitization compared with never cat ownership (adjusted odds ratio [OR_{adj}], 0.32; 95% confidence interval [CI], 0.14–0.74; $P = .01$). Early cat ownership was also associated with a significantly lower risk of allergic rhinitis than late cat ownership (OR_{adj}, 0.43; 95% CI, 0.22–0.85) or never cat ownership (OR_{adj}, 0.51; 95% CI, 0.28–0.92). No differences in the frequency of asthma were found among the 3 groups ($P = .74$).

Conclusions: Cat ownership in early childhood can play an important role in preventing sensitization to cat and in lowering the frequency of allergic rhinitis, at least in children with the characteristics of the population studied.

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INTRODUCTION

According to the “hygiene hypothesis,” the increased prevalence of allergic diseases in recent decades in Western countries might, at least partially, be explained by reduced exposure to microbes and endotoxins.¹ This view is somehow supported by the observations that the generational increase in allergic respiratory diseases seems to be lower in individuals who lived in a farming environment during childhood and that exposure to higher levels of house dust endotoxin in the first years of life is associated with a lower prevalence of sensitization.^{2,3} Because keeping dogs or cats at home is associated with higher exposure to endotoxin, it has been thought that pet ownership in childhood may drive immune development away from the T_H2 inflammatory response and therefore might contribute to the lower risk of allergic disorders later in life.⁴

Exposure to pets in the household, and particularly to cats, has been extensively studied and found to either decrease or increase the risk of sensitization and allergic diseases in

childhood.^{5–11} These discrepancies may be related to a variety of factors, including study design, population characteristics, and selection bias.¹² However, characteristics related to environmental, social, and lifestyle factors in the different countries or regions may affect not only the occurrence of pet ownership in the community but also the “intensity” of cat allergen exposure at home.^{13–15} With this background, the aim of the study was to evaluate the possible effects of cat ownership on the frequency of sensitization and allergic rhinitis or asthma in children with respiratory symptoms.

METHODS

Study Population and Methods

We enrolled 269 consecutive school-aged children referred by their primary care physicians for respiratory symptoms as outpatients to the Giannina Gaslini Institute in Genoa, Italy, in a 12-month period. Patient evaluation included personal and family medical histories, physical examination, and skin prick tests.^{16,17} The allergen panels tested included (1) house dust mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), (2) pollens (*Parietaria officinalis*, a mix of Graminae, and *Olea*), (3) pet dander (cat and dog skin allergen extracts), and (4) molds (*Alternaria tenuis*) (Bayropharm, Milan, Italy).

The diagnosis of asthma was defined in school-aged children by a consistent history or the demonstration of reversible bronchial obstruction with lung function testing according to

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Global Initiative for Asthma criteria,¹⁸ assessed at enrollment. The diagnosis of allergic rhinitis was based on repetitive sneezing, nasal itching, secretion, or obstruction apart from a cold episode.¹⁹

The presence or absence of cats in the home and the characteristics of cat ownership were evaluated by direct questioning by the physician. Children who had had a cat in their house but who did not have it at the time of evaluation were not included in the study. The “never” cat owner group included children who never had cats in their home, the “early” cat owner group included children who had a cat in their house in the first 2 years of life and still had it at the time of evaluation, and the “late” cat owner group included children who had a cat in their house after the first 2 years of life and still had it at the time of evaluation.

Information was also collected on other factors possibly related to atopy and respiratory symptom development, including family history of allergic disease (including history of rhinitis and asthma), exposure to passive smoking, number of siblings, and history of severe bronchiolitis in infancy. All the studied children lived in Liguria, a region on the northwestern sea coast of Italy with a typical Mediterranean climate. All the parents or caregivers gave their informed consent.

Statistical Methods

The quantitative variable (ie, age) is expressed and reported as median with lower and upper quartiles. Descriptive statistics for qualitative variables were first calculated and reported in terms of absolute frequencies and percentages. Comparison of the qualitative data between groups of patients was performed by means of the χ^2 test. The Bonferroni adjustment was applied as a correction for multiple comparisons to explore post hoc differences between pairs of groups.

To evaluate the roles of different independent explanatory variables in association with asthma, allergic rhinitis, and sensitization, a multiple logistic regression analysis was performed. Before the application of logistic regression procedures, age was dichotomized into a binary variable (<10 vs ≥ 10 years) based on the median value. The step-down strategy of analysis, which consists of examining the effect of removing variables from the saturated model, was chosen. Variables that were considered important for the outcome a

priori or that were statistically significant in the univariate analysis ($P < .05$) were entered into the model. The variables analyzed were sex, age category, family history of atopy, siblings, and cat ownership. The effect is expressed as adjusted odds ratio (OR_{adj}) with 95% confidence intervals (CIs). Statistical significance was tested using the likelihood ratio test. $P < .05$ was considered statistically significant. The statistical packages used were Statistica (StatSoft Corp, Tulsa, OK) for univariate analyses and Stata release 7 (Stata-Corp LP, College Station, TX) for multivariate analyses.

RESULTS

Demographic Characteristics of the Study Population

Of 269 children enrolled, 123 were never cat owners, 81 were early cat owners, and 65 were late cat owners. Most cat owners (95.1%) had only 1 cat at a time. The 3 groups were comparable in age and sex distribution (Table 1). No differences in the frequency of a family history of atopy were recorded among the 3 groups of children (Table 1). Of 269 children enrolled, 184 (68.4%) were sensitized to at least 1 aeroallergen, including cat allergen. The frequency of the allergic sensitizations in the whole population and in the 3 groups are shown in Figure 1.

Cat Ownership, Allergic Sensitization, and Respiratory Symptoms

Univariate analysis of the data showed that the proportion of children sensitized to at least 1 aeroallergen seemed to be lower in early cat owners than in late or never cat owners, without reaching statistical significance ($P = .06$) (Table 1). Logistic regression analysis was used to adjust for the effects of possible confounding variables on relationships between cat ownership and risks of sensitization. However, also after adjusting for family history of atopy and age category (<10 vs ≥ 10 years), the 3 groups of cat owners had the same risk of sensitization to aeroallergens ($P = .08$), although the risk tended to be lower in early cat ownership than in never (OR_{adj}, 0.50; 95% CI, 0.27–0.91) (Table 2).

In contrast, univariate analysis demonstrated a significant association between never owning a cat and increased sensitization to cat (Table 1). Indeed, the proportion of children sensitized to cat was significantly higher in never cat owners

Table 1. Univariate Analysis of the Relationship Between Cat Ownership and Some Demographic and Clinical Features in 269 Children

	Cat ownership			χ^2	P value
	Early (n = 81)	Late (n = 65)	Never (n = 123)		
Age, median (lower-upper quartiles), y	9 (8–11)	10 (9–12)	10 (8–11)	0.52	.77
Male sex, No. (%)	44 (54.3)	41 (63.1)	82 (66.7)	3.20	.20
Family history of atopy, No. (%)	42 (51.9)	33 (50.8)	73 (59.3)	1.73	.42
Allergic sensitization, No. (%)	48 (59.3)	44 (67.7)	92 (74.8)	5.47	.06
Cat sensitization, No. (%)	8 (9.9)	10 (15.4)	31 (25.2)	8.16	.02
Physician-diagnosed allergic rhinitis, No. (%)	27 (33.3)	35 (53.8)	62 (50.4)	7.80	.02
Physician-diagnosed asthma, No. (%)	46 (56.8)	35 (53.8)	63 (51.2)	0.61	.74

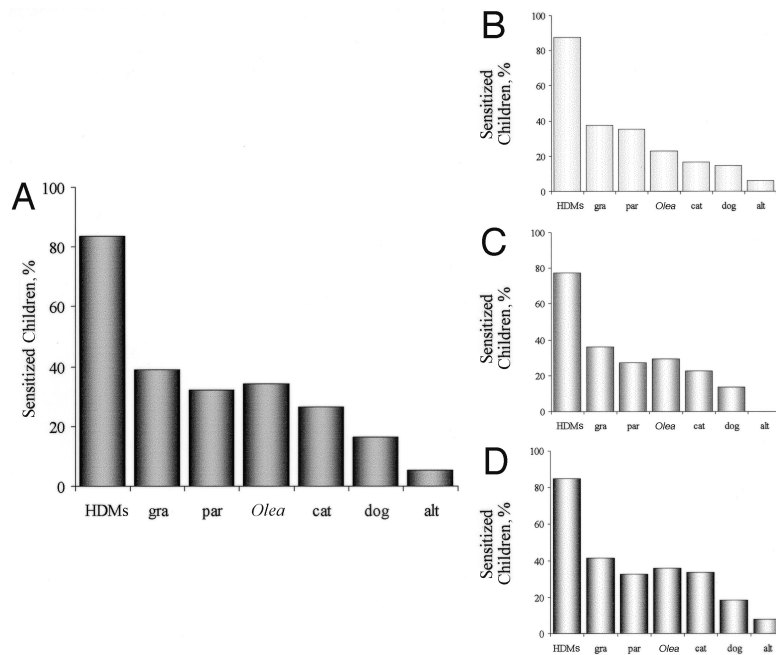


Figure 1. Distribution of allergic sensitization (house dust mites [HDMs], Graminae [gra], *Parietaria officinalis* [par], *Olea*, cat, dog, and *Alternaria tenuis* [alt]) in the whole population (A) and in each cat owner group: children who had a cat in their house in the first 2 years of life and still had it at the time of evaluation (“early” cat owners) (B), children who had a cat in their house after the first 2 years of life and still had it at the time of evaluation (“late” cat owners) (C), and children who never had cats in their home (“never” cat owners) (D).

than in early cat owners ($P = .02$). No differences were found between early and late cat owners ($P = .68$) or between late and never cat owners ($P = .32$). When logistic regression analysis adjusted for family history of atopy and age category was conducted, the association between increased risk of

sensitization to cat and never owning a cat remained significant ($P = .01$) (Table 2). Indeed, early cat ownership was associated with a significantly lower risk of sensitization to cat than never cat ownership (OR_{adj} , 0.32; 95% CI, 0.14–0.74; $P = .01$) (Table 2), whereas no differences were found

Table 2. Logistic Regression Models of Baseline Variables as Predictors of the 3 Study Outcomes in the Whole Study Population (N = 269)*

Outcome	Explanatory variables	OR _{adj} (95% CI)	P value
Allergic sensitization (no vs yes)	Cat ownership (never vs early)	0.50 (0.27–0.91)	.08
	Cat ownership (never vs late)	0.71 (0.37–1.38)	
	Cat ownership (late vs early)	0.70 (0.35–1.39)	
	Cat ownership (late vs never)	1.40 (0.72–2.73)	
	Family history of atopy (no vs yes)	1.16 (0.69–1.96)	
	Age category (<10 vs ≥10 y)	1.26 (0.75–2.12)	
Cat sensitization (no vs yes)	Cat ownership (never vs early)	0.32 (0.14–0.74)	.01
	Cat ownership (never vs late)	0.52 (0.23–1.15)	
	Cat ownership (late vs early)	0.62 (0.23–1.67)	
	Cat ownership (late vs never)	1.93 (0.87–4.27)	
	Family history of atopy (no vs yes)	0.75 (0.40–1.42)	
	Age category (<10 vs ≥10 y)	1.82 (0.95–3.48)	
Physician-diagnosed allergic rhinitis (no vs yes)	Cat ownership (never vs early)	0.51 (0.28–0.92)	.03
	Cat ownership (never vs late)	1.19 (0.64–2.20)	
	Cat ownership (late vs early)	0.43 (0.22–0.85)	
	Cat ownership (late vs never)	0.84 (0.45–1.56)	
	Family history of atopy (no vs yes)	1.60 (0.97–2.63)	
	Age category (<10 vs ≥10 y)	1.74 (1.06–2.85)	

Abbreviations: CI, confidence interval; OR_{adj}, adjusted odds ratio.

*The first category of each variable reported in parentheses is the reference category.

between early and late cat owners (OR_{adj} , 0.62; 95% CI, 0.23–1.67) or between never and late cat owners (OR_{adj} , 0.52; 95% CI, 0.23–1.15) (Table 2).

Univariate analysis also showed that the frequency of allergic rhinitis was different in the 3 groups ($P = .02$) (Table 1), being significantly lower in early cat owners than in late ($P = .04$) or never ($P = .048$) cat owners, whereas the frequency in allergic rhinitis was similar in late and never cat owners ($P = .96$). The relationship between cat ownership and physician-diagnosed allergic rhinitis remained significant, as demonstrated by logistic regression analysis adjusted for family history of atopy and age category ($P = .03$) (Table 2), with early cat ownership being associated with a significantly lower risk of physician-diagnosed allergic rhinitis than never cat ownership (OR_{adj} , 0.51; 95% CI, 0.28–0.92) or late exposure to cat (OR_{adj} , 0.43; 95% CI, 0.22–0.85) (Table 2). Risk of physician-diagnosed allergic rhinitis was not significantly different between late and never cat owners (OR_{adj} , 1.19; 95% CI, 0.64–2.20) (Table 2). No differences in the frequency of asthma were found among the 3 groups (Table 1).

DISCUSSION

The main finding is that only early cat ownership is protective against sensitization to cat and allergic rhinitis, at least in the population studied. The protective role of early cat ownership against sensitization to inhaled allergens in general, other than cat-derived allergens, or against asthma did not reach statistical significance.

A possible limitation of this study is that the group evaluated included only children with respiratory symptoms. Therefore, this group of children is not representative of the general pediatric population living in Liguria, and this may explain the high frequency (>50%) of patients sensitized to airborne allergens.¹⁷ Indeed, studies^{16,17} of school-aged children have disclosed a frequency of sensitization to aeroallergens in Liguria of 25% to 34%. Another possible confounding factor in this study could be the decision against pet ownership by parents of children with respiratory symptoms or a family history of atopy. However, this hypothesis seems unlikely because the percentage of never cat owners (45.7%) in our study population was considerably lower than the average reported in “continental” northern Italy,²⁰ and no difference in the frequency of a family history of atopy was observed among early, late, and never cat owners. This relatively high percentage of families feeding cats at their house may also be related to the fact that cats living in the streets are common in Liguria and in many regions on the European Mediterranean coasts. However, our findings are similar to those reported in a recent study²¹ performed in US homes.

The results presented herein are in agreement with most of the recent studies that have shown that exposure to pets, and specifically to cats, early in infancy may somehow reduce the prevalence of specific sensitization or allergic symptoms later in childhood. As stated by a recent review,²² this general trend is relatively consistent, although there are differences in specific findings between studies.

The methodological problems are complex and include not only the study design but also variables related to the intensity of allergen exposures and other environmental exposures (ie, climate, housing conditions, family, and social lifestyle).^{22,23} In Liguria, most families live in apartment buildings, and, therefore, keeping cats indoors is a common habit, in contrast to what is described in other countries.^{24,25} Indeed, high exposure to cat allergen has been associated with a lower prevalence of sensitization to cat compared with moderate exposure²⁶ and with the presence of a modified T_H2 response, producing IgG1 and IgG4 specific antibodies rather than IgE.^{27,28} Although we did not measure the level of exposure, we know that most homes with cats have Fel d 1 levels greater than 8 $\mu\text{g/g}$,^{26–28} and this level represents the strongest predictor of IgG1 and IgG4 antibody responses. The hypothesis of a switch of the T_H1/T_H2 response due to high cat allergen exposure in infancy is in agreement with our results, showing a protective role of early cat ownership against sensitization to cat.

An alternative hypothesis is that the protective effect of exposure to cats against the development of sensitization may also be caused by the effect of bacterial endotoxins, derived from the cat, that may come in close physical contact with children.^{3,29} Indoor endotoxin exposure early in life may be protective against allergen sensitization by enhancing type 1 immunity because endotoxin levels in the home may be directly related to interferon- γ production by T_H1 lymphocytes.³⁰ However, this primary mechanism of protection toward T_H2 responses would have determined a lower prevalence of sensitization to allergens other than cat. Indeed, our study shows a trend toward less sensitization to inhaled allergens in the early cat exposure group, although not statistically significant. A similar observation can be made in relation to the proposed hypothesis that high doses of cat allergen, such as those present in cat owners' houses, may induce a T-cell regulatory response, resulting in the production of cytokines such as interleukin 10 and transforming growth factor β , which play a key role in controlling allergic diseases and asthma.^{31,32}

We also found that early cat ownership seems to be protective against allergic rhinitis but not against asthma. The effect of early exposure to cats on nasal symptoms might be related to a deposition of greater amounts of allergen (and, eventually, of pet-derived endotoxins) on the upper airway mucosa, possibly leading to antigen tolerance. This phenomenon has been thought to have a key role during “mucosal” immunotherapy against grass pollen, in which high allergen loading results in stimulation of antigen-presenting cells and local production of “suppressive” cytokines such as transforming growth factor β or interleukin 10 from T-regulatory cells.^{33,34} The more effective protection of early vs late cat ownership against allergic rhinitis is consistent with the hypothesis that antigen tolerance and endotoxin-induced protection against allergic sensitization and allergic rhinitis may occur in the first 1 to 2 years of life.^{1,2,7,10}

In summary, these results suggest, at least in children with the characteristics of the population studied, that cat owner-

ship in childhood seems to reduce the risk of sensitization to inhaled allergens, even in children with a familial history of atopy. In addition, exposure to cats at home in early childhood seems to play a significant role in preventing sensitization to cat and in lowering the risk of allergic rhinitis.

REFERENCES

1. von Mutius E. Infection: friend or foe in the development of atopy and asthma? the epidemiological evidence. *Eur Respir J*. 2001;18:872–881.
2. Holla AD, Roy SR, Liu AH. Endotoxin, atopy and asthma. *Curr Opin Allergy Clin Immunol*. 2002;2:141–145.
3. Gehring U, Bischof W, Fahlbusch B, et al. House dust endotoxin and allergic sensitization in children. *Am J Respir Crit Care Med*. 2002;166:939–944.
4. Heinrich J, Gehring U, Douwes J, et al. Pets and vermin are associated with high endotoxin levels in house dust. *Clin Exp Allergy*. 2001;31:1839–1845.
5. Pearce N, Pekkanen J, Beasley R. How much asthma is really attributable to atopy? *Thorax*. 1999;54:268–272.
6. 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.
7. Hesselmar B, Aberg N, Aberg B, et al. Does early exposure to cat or dog protect against later allergy development? *Clin Exp Allergy*. 1999;29:611–617.
8. Ownby DR, Johnson CC, Peterson EL. Exposure to dogs and cats in the first year of life and risk of allergic sensitization at 6 to 7 years of age. *JAMA*. 2002;288:963–972.
9. Lau S, Illi S, Sommerfeld C, et al. Early exposure to house-dust mite and cat allergens and development of childhood asthma: a cohort study. *Lancet*. 2000;356:1392–1397.
10. Custovic A, Simpson BM, Simpson A, et al. Effect of environmental manipulation in pregnancy and early life on respiratory symptoms and atopy during first year of life: a randomised trial. *Lancet*. 2001;358:188–193.
11. Almqvist C, Egmar AC, Hedlin G, et al. Direct and indirect exposure to pets: risk of sensitization and asthma at 4 years in a birth cohort. *Clin Exp Allergy*. 2003;33:1190–1197.
12. Brunekreef B, Groot B, Hoek G. Pets, allergy and respiratory symptoms in children. *Int J Epidemiol*. 1992;21:338–342.
13. Custovic A, Woodcock A. Exposure and sensitization in infants and children. *Curr Opin Allergy Clin Immunol*. 2001;1:133–138.
14. Custovic A, Murray CS. The effect of allergen exposure in early childhood on the development of atopy. *Curr Allergy Asthma Rep*. 2002;2:417–423.
15. von Mutius E. Influences in allergy: epidemiology and the environment. *J Allergy Clin Immunol*. 2004;113:373–379.
16. Silvestri M, Rossi GA, Cozzani S, et al. Age-dependent tendency to become sensitized to other classes of aeroallergens in atopic asthmatic children. *Ann Allergy Asthma Immunol*. 1999;83:335–340.
17. Strachan D, Sibbald B, Weiland S, et al. Worldwide variations in prevalence of symptoms of allergic rhinoconjunctivitis in children: the International Study of Asthma and Allergies in Childhood (ISAAC). *Pediatr Allergy Immunol*. 1997;8:161–176.
18. Global Initiative for Asthma. *Global Strategy for Asthma Management and Prevention*. Bethesda, MD: National Institutes of Health, National Heart, Lung, and Blood Institute; February 2002. NIH publication 02–3659.
19. Bousquet J; ARIA Workshop Group. Allergic Rhinitis and its Impact on Asthma (ARIA). *J Allergy Clin Immunol*. 2001;108:S147–S336.
20. Pescolderrung L, Pietrobelli A, Boner AL. Cat sensitivity: 7-yr audit in children attending a paediatric allergy clinic in North Italy. *Eur Respir J*. 2000;16:857–860.
21. Arbes SJ Jr, Cohn RD, Yin M, et al. Dog allergen (Can f 1) and cat allergen (Fel d 1) in US homes: results from the National Survey of Lead and Allergens in Housing. *J Allergy Clin Immunol*. 2004;114:111–117.
22. Ownby DR, Johnson CC. Does exposure to dogs and cats in the first year of life influence the development of allergic sensitization? *Curr Opin Allergy Clin Immunol*. 2003;3:517–522.
23. Apter AJ. Early exposure to allergen: is this the cat's meow, or are we barking up the wrong tree? *J Allergy Clin Immunol*. 2003;111:938–946.
24. Gulbahar O, Sin A, Mete N, et al. Sensitization to cat allergens in non-cat owner patients with respiratory allergy. *Ann Allergy Asthma Immunol*. 2003;90:635–639.
25. Fahlbusch B, Gehring U, Richter K, et al. Indoor factors and genetics in asthma. *J Invest Allergol Clin Immunol*. 2002;12:12–20.
26. Custovic A, Hallman CL, Simpson BM, et al. Decreased prevalence of sensitization to cats with high exposure to cat allergen. *J Allergy Clin Immunol*. 2001;108:537–539.
27. Platts-Mills TA, Perzanowski M, Woodfolk JA, Lundback B. Relevance of early or current pet ownership to the prevalence of allergic disease. *Clin Exp Allergy*. 2002;32:335–338.
28. Hesselmar B, Aberg B, Eriksson B, et al. High-dose exposure to cat is associated with clinical tolerance: a modified Th2 immune response? *Clin Exp Allergy*. 2003;33:1681–1685.
29. Park JH, Gold DR, Spiegelman DL, et al. House dust endotoxin and wheeze in the first year of life. *Am J Respir Crit Care Med*. 2001;163:322–328.
30. Gereda JE, Leung DY, Thatayatikom A, et al. Relation between house-dust endotoxin exposure, type 1 T-cell development, and allergen sensitization in infants at high risk of asthma. *Lancet*. 2000;355:1680–1683.
31. Umetsu DT, Akbari O, Dekruyff RH. Regulatory T cells control the development of allergic disease and asthma. *J Allergy Clin Immunol*. 2003;112:480–487.
32. Jutel M, Akdis M, Budak F, et al. IL-10 and TGF- β cooperate in the regulatory T cell response to mucosal allergens in normal immunity and specific immunotherapy. *Eur J Immunol*. 2003;33:1205–1214.
33. Francis JN, Till SJ, Durham SR. Induction of IL-10+CD4+CD25+ T cells by grass pollen immunotherapy. *J Allergy Clin Immunol*. 2003;111:1255–1261.
34. Nouri-Aria KT, Wachholz PA, Francis JN, et al. Grass pollen immunotherapy induces mucosal and peripheral IL-10 responses and blocking IgG activity. *J Immunol*. 2004;172:3252–3259.

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