ORITINAL ARTICLE

UDC: 616-056.43:616.211-022
https://doi.org/10.2298/VSP170309071B

Incidence of sensitization to specific inhalatory allergens in patients suffering from allergic rhinitis

Učestalost senzibilizacije na pojedine inhalatorne alergene kod obolelih od alergijskog rinitisa

Maja Buljčik Čupić*†, Slobodan Savović*†, Sanja Hromiš*‡, Slobodanka Lemajić Komazec*†, Dea Karaba Jakovljević§

University of Novi Sad, *Faculty of Medicine, §Department of Physiology, Novi Sad, Serbia; Clinical Center of Vojvodina, †ENT Clinic, Novi Sad, Serbia; ‡Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica, Serbia

Abstract

Backgound/Aim. Allergic rhinitis is the most frequent type of rhinitis affecting more than 600 million people worldwide. As incidence increases, it is important to know about the characteristics, the allergens that exacerbate it as well as effects of allergic rhinitis on population. The aim of this study was to determine among patients with chronic rhinitis the number of patients positive to standard inhaled allergens, their distribution by sex, age and to determine the type and frequency of allergic sensitization to specific inhalatory allergens. **Methods.** Data was collected from 514 patients tested for standard inhalatory allergens via the skin prick test from 01.01.2016 to 31.12. 2016. Age, sex and concomitant diseases as well an analysis of type and frequency of hypersensitivity to different allergens were assessed and recorded. **Results.** Of 514 patients, 307 patients, with an average age of 29.6 ± 8.88 years had a positive skin prick test. The sex ratio was 1.2 : 1 in favor of the females. Outdoor allergens affected 81.2% of all patients while indoor allergens 66.4% of them. Weed pollen (71%), grass pollen (61%) and *Dermatophagoides pteronyssinus* (46%) were the most common allergens. Most patients were sensitized to 1 (22%) or 2 (22%) allergens, while 20% of patients were simultaneously sensitized to 3 allergens. **Conclusion.** Most patients with the symptoms of chronic rhinitis had a positive allergic reaction. Those in their third decade of life were the most commonly affected. Outdoor allergens were the most prevalent allergen group, and weed pollen was the most frequent type of allergen.

Key words:
rhinitis, alleric; allergens; plant weeds; dermatophagoides pteronissinus; incidence; intradermal tests.

Apstrakt

Uvod/Cilj. Alergijski rinitis kao najčešći oblik hroničnog zapaljenja sluznice nosa (rinitisa), nalazi se na četvrtom mestu na listi najčešćih hroničnih oboljenja na svetu, s obzirom da od njega boluje više od od 600 miliona ljudi. Zbog izuzetno brzog porasta incidence oboljenja, značajno je odrediti karakteristike inhalatornih alergena koji ga izazivaju kao i efekte samog oboljenja na populaciju. Cilj studije je bio da se u grupi obolelih od hroničnih rinitisa, koji se podvrgavaju testiranju na alergije, utvrdi broj onih koji su alergični, njihova distribucija po polu, starosti i utvrđivanje vrste i učestalosti alergijske senzibilizacije na specifične inhalatorne alergene. **Metode.** Prospektivo-retrospektivnom studijom analizirani su podaci 514 pacijenata sa hroničnim rinitisom, koji su podvrgnuti testiranju na alergije, supkutanim testom uz upotrebu standardnih inhalatornih alergena, u periodu od godinu dana (od 1.01.2016 do 31.12.2016). Analizirani su starost, pol, pridružene bolesti ispitanika sa alergijskim rinitisom, kao i vrsta i učestalost hipersenzibilizacije na pojedine alergene. **Rezultati.** Od 514 pacijenata sa hroničnim rinitisom, 307 pacijenata prosečne starosti od 29.6 ± 8.88 godina i blagom dominacijom ženskog pola u odnosu na muški (1,2 : 1) je imalo pozitivan test na inhalacione alergene. Na spoljašnje alergene je bilo senzibilisano 81.2% pacijenata, a na unutrašnje alergene 66.4%. Dominantna senzibilizacija bila je na polen korova (71%), polen trava (61%) i na grinje (*Dermatophagoides pteronyssinus*) (46%). Većina pacijenata bila je senzibilisana na 1 (22%) ili 2 (22%) alergena, dok je istovremeno na tri alergena bilo senzibilisano 20% pacijenata. **Zaključak.** Većina pacijenata sa simptomima hroničnog rinitisa je imala pozitivan test na alergije. Najčešće su to pacijenti u trećoj deceniji života. Spoljni alergeni sa najvećom prevalencom uzrokuju alergijski rhinitis, i to dominantno polen korova.

Ključne reči:
rinitis, alerijski; alergeni; korovi; dermatophagoides pteronisssinus; incidenca; intradermalni testovi.

Correspondence to: Maja Buljčik Čupić, Clinical Center of Vojvodina, ENT Clinic, Hajduk Veljkova 1, 21 137 Novi Sad, Serbia.
E-mail: majabuljcik@gmail.com

Introduction

With over 10 million appointments scheduled annually, allergic rhinitis (AR) is a global health problem and one of the most common reasons to visit a doctor. AR is the most frequent type of rhinitis, an inflammation of the nasal pathways initiated by an allergic immune response to inhaled allergens in sensitized individuals. Seasonal allergic rhinitis is caused by outdoor allergens while perennial allergic rhinitis is caused by indoor allergens such as dust mites, pet dander and mould. The signs and symptoms of AR are numerous, often presented with rhinorrhea (excess nasal secretion), itching, nasal congestion and obstruction.

According to the World Health Organization, AR is in the fourth place regarding frequency of chronic disease and more than 600 million people suffer from it - 20%–30% of the population with a steady increase in prevalence. Shockingly enough, 17%–23% of patients do not even know that they have AR. In the EU countries, the prevalence of this disease is 22.7%, according to the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines [1–8].

In 80% of patients, AR develops before 20 years of age. Sometimes symptoms appear in individuals when they reach their third decade of life [8]. Although this is a disease that is not life-threatening, it must be mentioned that it does significantly affect one's quality of life by causing a number of symptoms that are not directly related to AR such as fatigue, agitation, insomnia, hearing loss, anxiety, nausea, feelings of sadness and depression [1–4]. In children especially, symptoms of agitation and hypersensitivity tend to dominate during the day. About 50% of patients report having symptoms of AR more than 4 months out of the year and 20% of sufferers have symptoms more than 9 months throughout the year. This has a significant impact as these disturbances may prevent individuals from being able to do daily necessities such as going to work or school [9].

Approximately 15%–20% of general practitioners do not consider AR as a disease that needs to be treated, however AR provides a "foundation" or risk of developing a number of other conditions and diseases such asthma, rhinitis, chronic rhinosinusitis with nasal polyps (CRSwNP) and inflammation of the middle ear which further increases its medical significance as well as its treatment costs which have been estimated to be around 510 million euros. Patients with AR have more episodes of acute respiratory infections of the upper respiratory tract which in turn last longer and have a graver course of the disease [10, 11].

In turn, early detection and treatment is the key to prevention of the graver course of disease.

The aim of this study was to determine the number of patients with a positive allergic reaction to standard inhalatory allergens, tested by means of the skin prick test as well as their distribution by sex, age and to determine the type and frequency of allergic sensitization to specific inhalatory allergens among those patients.

Methods

This study was designed as a retrospective-prospective investigation. The data was collected in the tertiary level clinic, from medical histories of patients for the period from January 1st, 2016 to December 31st, 2016. In total, 514 patients with the presumptive diagnosis of allergic rhinitis, were sent to do a skin prick test to confirm their atopic status after having undergone a clinical ear, nose and throat (ENT) examination. The skin prick test is performed according to the recommendations of the Subcommittee on Skin Tests of the European Academy of Allergy and Clinical Immunology (EAACI) [1, 2]. The standard solutions of inhalatory allergens from the Institute of Virology, Vaccines and Serums "Torlak" in Belgrade were used (house dust, *Dermatophagoides pteronyssinus*, linen, animal hair, dog hair, cat hair, cockroaches, feathers, cigarette smoke, fungus (mould), bacteria, pollen of trees, grass pollen and weed pollen). Positive skin prick test was marked as the diameter of reaction that is 3 mm higher than the negative control.

After the confirmation of the allergic disease in the total number of patients, an estimate of age, sex and concomitant diseases was done. In the patients with the positive allergy tests, we performed an analysis of type and frequency of hypersensitivity to standard inhalatory allergens.

The data was statistically processed by the Microsoft Excel 2010 software for statistical and tabular calculations. The organized data was then placed into the program STATISTICA 7 for calculation of the descriptive statistical parameters (sum, mean, minimum and maximum and standard deviation) and presented in the results section.

Results

During the 2016, 514 patients with suspected AR underwent the skin prick test for the standard inhalatory allergens. Of 514 patients that exhibited signs and symptoms of AR, 307 (59.7%) had a positive skin prick test, while 207 patients were negative and excluded from further testing. Within the 307 sensitized patients, the average age was 29.6 ± 8.88 years. The youngest patient was 13 years old and the oldest one was 64 years old. Females represented 167/307 (54.4%) and males 140/307 (45.6%) of the patients, with the positive test results to standard inhalatory allergens. The sex ratio was 1.2 : 1 in favour of the females. In this study, we also compared the number of patients that had at least one or more comorbidities along with AR to the positively tested patients who had no other diagnosis. The patients with comorbidities made up 295/307 (96.1%). The most common comorbidities observed were nasal septum deviation, conjunctivitis, acute and chronic rhinosinusitis, bronchial asthma, chronic rhinosinusitis with nasal polyps (CRSwNP), and medicamentous chronic rhinitis.

After dividing the standard inhalatory allergens into three groups of indoor, outdoor and combined allergens, sensitization to individual indoor allergens was present in 58/307 (18.8%) patients while the sensitization to collective indoor allergens was present in 66.4% of all patients. Sensitization to individual outdoor allergens was present in 103/307 (33.6%) patients, while sensitization to collective ones was present in 81.2% of all patients. The results of the combined outdoor/indoor allergen group were present in 146/307 (47.6%) patients (Figure 1).

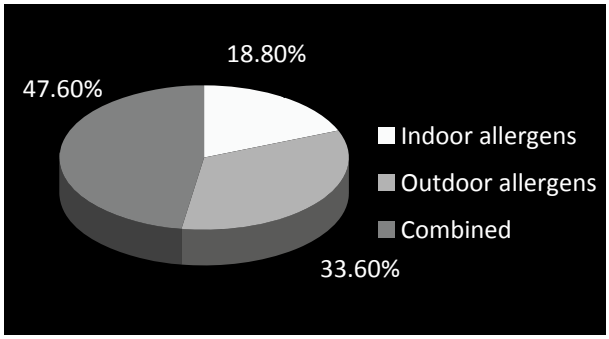

Fig. 1 – Percentage of the patients with indoor, outdoor and combined allergens.

After assessing patients hypersensitivity to each allergen, 222/307 (72%) patients were sensibilized to weed pollen, with grass pollen as the second most common allergen presenting 187/307 (61%) participants while *Dermatophagoides pteronyssinus* was the third most common allergen with a result of 141/307 (46%). Tree pollen also had a significant result in 125/307 (41%) patients as did house dust, affecting 113/307 (37%) patients. The rest of the standard inhalator allergens were considerably less frequent among the participants. Allergy to linen was found in 45 (15%) of the patients, to bacteria in 28 (9%), to cockroaches in 27 (9%), to mould in 25 (8%), to animal hair in 21 (7%), to cigarette smoke in 18 (6%), to feathers in 15 (5%), to cat hair in 12 (4%) and lastly, to dog hair in 9 (3%) of the patients (Figure 2).

When observing hypersensitivity to the number of allergens in each patient, the greatest number of patients were sensitized to one allergen 67/307 (22%), then 67/307 (22%) to two allergens while 62/307 (20%) were sensitized to three allergens. Hypersensitivity was significantly lower in the patients polysensitized to four 43/307 (14%), five 31/307 (10%), six 16/307 (5%), seven 8/307 (3%) and eight 7/307 (2%) allergens. Sensitization to nine, eleven, thirteen and fourteen allergens was the same, 1/307 (0.4%), while there was no patients who were simultanously allergic to twelve allergens (Figure 3).

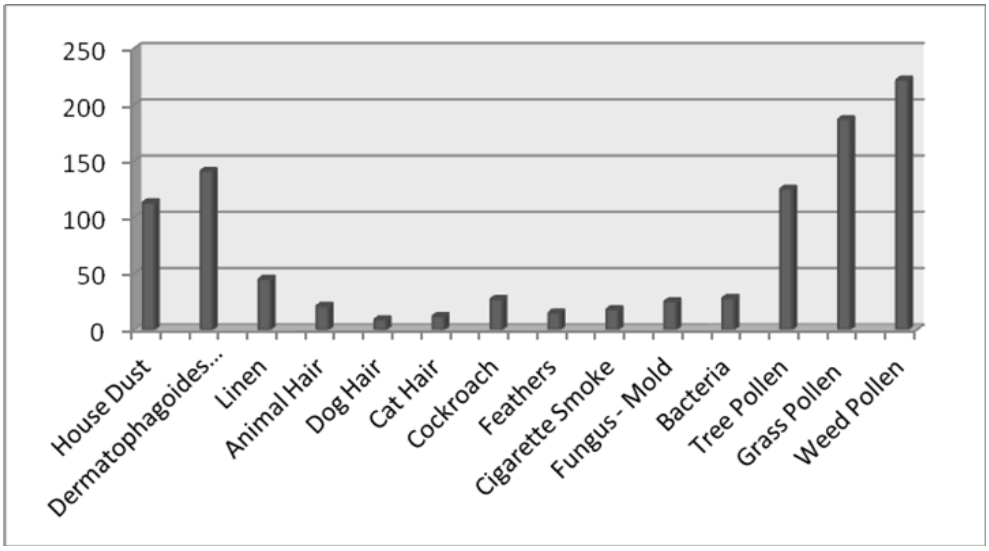

Fig. 2 – Number of patients allergic to each allergen.

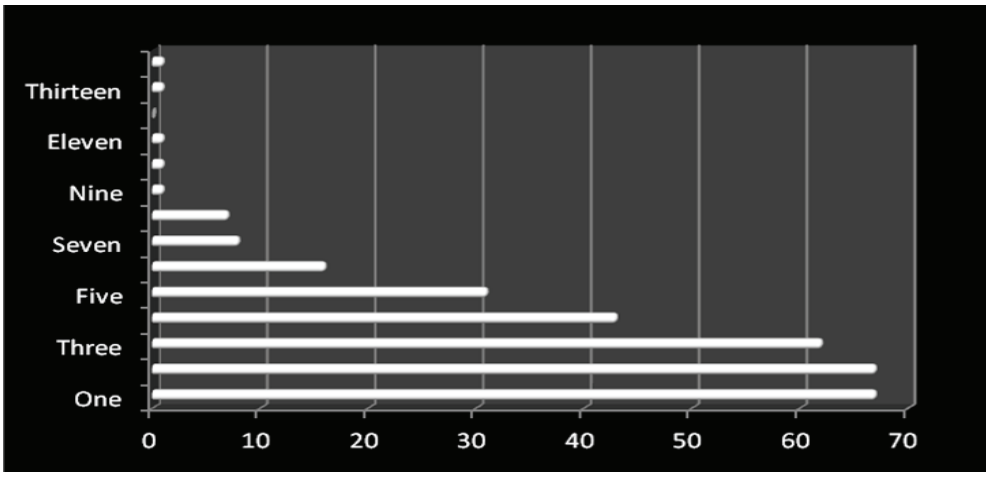

Fig. 3 – Distribution of the patients allergic to one or more allergens.

Discussion

AR is the most common type of allergy in Europe, affecting from 17% to 28% of the European population. That being said, the incidence of AR may vary among as well as within countries themselves. Of the 514 patients who underwent testing for standard inhalatory allergens in 2012, 59.7% of them tested positive, giving a majority. However, it is important to emphasize that a portion of those patients who did not have a positive skin prick test may develop AR over time which is confirmed by studies on the subject of local allergic rhinitis [12–15]. According to a study by Rondon et al. [16], local allergic rhinitis is a newly described type of rhinitis where a local allergic response exists in nasal mucosa, characterized by the production of specific immunoglobulin E (sIgE) antibodies in the absence of atopy (genetic predisposition to increased production of IgE antibodies). It can affect the patients who have been previously diagnosed with non-allergic rhinitis. For the patients with negative results for the skin prick test but symptoms suggestive for AR, an advanced diagnostic approach was proposed with the detection of local sIgE in nasal secretions during natural exposure to inhalatory allergens and a positive allergen provocation test with increased local production of tryptase, eosinophil cationic protein (ECP) and sIgE.

Other studies have proven that gender does seem to have an impact on the prevalence of AR. In childhood, allergic rhinitis is more common in boys than in girls, however, more interestingly, the prevalence is approximately equal between men and women. This information correlates with our results that determined that the women make up 54.4% of positive patients while the men make up 45.6%, giving the ratio of 1.2: 1.

The results of our study demonstrated that the average age was 29.7 years with a standard deviation of ± 8.88 years. Other studies showed that the mean age of onset in childhood was 8–11 yearsof age, but AR may occur in persons of any age. In 80% of affected individuals, AR developed by the age of 20.

AR does not typically present itself as just a single disease. It it is often associated with numerous other pathologies. As it was proven by our results, 96.1% of positively tested patients had a coexisting morbidity. In a study by Zvezdin et al. [17], 74.1% of all patients had at least one concomitant disease. This data correlates with the results of our study, showing that the majority of patients have a comorbidity along with AR. The most common concomitant diseases were septal deviation, conjunctivitis, chronic rhinosinusitis with or without polyps, long lasting dry caught, gastroesophageal reflux disease (GERD), asthma and bronchial hyperactivity.

Analysis of the frequency and type of sensitization to standard inhalatory allergens is extremely significant since exposure to aeroallergens contributes to both the exacerbation of the symptoms and the formation of the disease itself. The standard inhalatory allergens that were used in the skin prick test can be categorized into three groups: indoor, outdoor and combined allergens. Indoor allergens include house dust, *Dermatophagoides pteronyssinus*, linen, animal hair, dog hair, cat hair, cockroaches, feathers, cigarette smoke, fungus (mould) and bacteria. Outdoor allergens are weed pollen, grass pollen and tree pollen, while combined allergens include both type of allergens. As far as our results are concerned, indoor allergens alone comprised 18.8% of patients, while combined indoor allergens made up 66.4% of the patients. Outdoor allergens make up 33.6% alone, although combined outdoor allergens make up 81.2% of the patients. Combined allergens comprised 47.6% of a total number of the patients. In a similar study, participants were hypersensitive to combined indoor allergens in 77.5% of cases, while 67.6% were positive to combined outdoor allergens. Hypersensitivity to both allergen types (combined allergens) was verified in 48.4% of patients. When interpreting the results of both studies, it was established that indoor allergens were more frequent in the other study while outdoor allergens were predominant in ours. The results of combined allergens were approximately the same [17, 18]. An international study done by the European Community Respiratory Health Survey (ECRHS) noted that different external factors which influence the prevalence of rhinitis and atopy were determined by the geographical features of a particular environment. For instance, our study confirmed that the most common pollen allergen in the region of Vojvodina was weed pollen. However, in the northern European countries, tree pollen was pointed out to be the most common allergen. Similarly, hypersensitivity to grass pollen was most frequent in the majority of other European countries. Thus, it can be said that sensitization to pollens is different in regions all over Europe depending on characteristics of that region such as vegetation and climate. Social factors within certain environment should also be taken into account when comparing the incidence of specific allergens among regions. Hypersensitivity to cat hair, for example, affected a relatively insignificant number of patients contributing to only 4% of all allergens, while some studies show that cat hair is the most common allergen in the adult population and in children with rhinitis and/or asthma, ranging from 15%–50% in western countries. The reasoning behind this information may be attributed to the cat being the most common pet in these environments [17, 18].

Our research showed that 72% of the patients were sensitized to weed pollen, making it the most common allergen among all pollens, outdoor allergens as well as all standard inhalatory allergens. Grass pollen is the second most common allergen, comprising 61% of total allergens. *Dermatophagoides pteronyssinus* is the third most common allergen when taking into account all allergens in total with a result of 46%; however, it is by far the most common indoor allergen. Our results are in accordance with the results of another studies that confirm that weed pollen is the most common outdoor allergen and that *Dermatophagoides pteronyssinus* is the most common indoor allergen. It is also important to mention that pollens, when calculated together, compose 34% of all standard inhalatory allergens [17, 18].

When observing hypersensitivity of each pateient to the number of allergens, it was established that 22% of individuals were allergic to only one allergen. Interestingly enough, the same result was observed in individuals who were allergic to two allergens, whereas slightly fewer patients (20%) were allergic to three allergens. In those hypersensitive to more allergens, the frequency and percentage of the participants decreased.

Conclusion

The majority of the patients tested via the skin prick method had a positive allergic reaction to standard inhalator allergens. Those in their third decade of life were the most commonly affected, with the female population being slightly predominant. Outdoor allergens were the prevalent group of allergens, with weed pollen as the most frequently found type of allergen within the population.

REFERENCES

1. *Akdis CA, Peter W, Hellings PW, Agache I.* Global atlas of allergic rhinitis and chronic rhinosinusitis. Zurich, Switzerland: European Academy of Allergy and Clinical Immunology; 2015.
2. *Akdis CA, Agache I.* Global atlas of asthma. Zürich: EAACI; 2013.
3. *Shedden A.* Impact of nasal congestion on quality of life and work productivity in allergic rhinitis: Findings from a large online survey. Treat Respir Med 2005; 4(6): 439–46.
4. *Ciprandi G, Klersy C, Cirillo I, Marseglia GL.* Quality of life in allergic rhinitis: relationship with clinical, immunological, and functional aspects. Clin Exp Allergy 2007; 37(10): 1528–35.
5. *Schatz M.* A survey of the burden of allergic rhinitis in the USA. Allergy 2007; 62(Suppl 85): 9–16.
6. *Canonica GW, Bousquet J, Mullol J, Scadding GK, Virchow JC, Manns J,* et al. A survey of the burden of allergic rhinitis in Europe. Allergy 2007; 62(85): 17–25.
7. *Bauchau V, Durham SR.* Prevalence and rate of diagnosis of allergic rhinitis in Europe. Eur Respir J 2004; 24(5): 758–64.
8. *Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A,* et al.Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy 2008; 63 Suppl 86: 8–160.
9. *Ciprandi G, Tosca MA, Fasce L.* Allergic children have more numerous and severe respiratory infections than non-allergic children. Pediatr Allergy Immunol 2006; 17(5): 389–91.
10. *Cirillo I, Marseglia G, Klersy C, Ciprandi G.* Allergic patients have more numerous and prolonged respiratory infections than nonallergic subjects. Allergy 2007; 62(9): 1087–90.
11. *Bielory L.* Allergic conjunctivitis and the impact of allergic rhinitis. Curr Allergy Asthma Rep 2010; 10(2): 122–34.
12. *Fokkens W, Lund V, Bachert C, Clement P, Helllings P, Holmstrom M,* et al. EAACI Position Paper on Rhinosinusitis and Nasal Polyps Executive Summary. Allergy 2005; 60(5): 583–601.
13. *Scadding GK, Durham SR, Mirakian R, Jones NS, Leech SC, Farooque S*, et al. BSACI guidelines for the management of allergic and non-allergic rhinitis. Clin Exp Allergy 2008; 38(1): 19–42.
14. *Scadding GK.* Allergic rhinitis: background, symptoms, diagnosis and treatment options. Nurs Times 2009; 105(30): 24–7.
15. *Greiner AN, Hellings PW, Rotiroti G, Scadding GK.* Allergic rhinitis. Lancet 2011; 378(9809): 2112–22.
16. *Rondon C, Fernandez J, Canto G, Blanca M.* Local Allergic Rhinitis: Concept, Clinical Manifestions, and Diagnostic Approach. J Investig Alllerog Clin Immunol 2010; 20(5): 364–71.
17. *Zvezdin B, Milutinov S, Tanasković I, Kojicić M, Kolarov V, Hromis S,* et al. The frequency of sensitization to inhalatory allergens and concomitant rhinitis in asthmatic patients. Vojnosanit Pregl 2011; 68(4): 309–13.
18. *Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A,* et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy 2008; 63 Suppl 86: 8–160.

Received on March 9, 2017.
Revised on April 27, 2017.
Accepted on April 27, 2017.
Online First May, 2017.