

Efficacy evaluation of a pollen blocker cream against dust-mite allergy: A multicenter, randomized, double-blind, placebo-controlled crossover trial

Yanqing Li, M.D.,¹ Lei Cheng, M.D.,² Xiaoning Chen, M.D.,³ Beibei Yang, M.D.,⁴ and Dehui Wang, M.D.¹

ABSTRACT

Objective: To further evaluate the efficacy and safety of a pollen blocker cream against dust-mite allergy.

Methods: A multicenter, randomized, double-blind, placebo-controlled, crossover trial was conducted in a Chinese population. Patients diagnosed with perennial allergic rhinitis, sensitive to dust-mite allergy including *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* were randomly allocated to receive a pollen blocker cream or placebo, which was applied and spread evenly to the lower internal nose region three times daily for a total of 30 days. The primary outcome measurements for efficacy were total nasal symptom score (TNSS) and individual nasal symptom score (iNSS). Adverse events were also monitored.

Results: After application of a pollen blocker, the mean TNSS decreased from 23.1 to 13.8, the decrease of the pollen blocker group (9.3) was highly significant compared with the placebo group (5.2; $p < 0.001$). Similarly, the decreases in iNSSs (rhinorrhea, congestion, sneezing, and itching) between the pollen blocker group and the placebo group were also significant ($p < 0.05$). In addition, in adults, the pollen blocker led to a remarkably significant decrease in TNSS (9.5) compared with placebo (5.4; $p < 0.001$); in children, the pollen blocker led to a significant decrease in TNSS (8.6) compared with placebo (4.8; $p < 0.05$). No statistical difference was found in the incidence of adverse events between the two groups ($p > 0.05$), and no severe systematic reactions were observed.

Conclusion: Pollen Blocker is a safe and effective alternative to the drugs for treatment of AR, especially for Chinese people allergic to dust-mite allergy. (Am J Rhinol Allergy 29, e129–e133, 2015; doi: 10.2500/ajra.2015.29.4218)

Allergic rhinitis (AR) is an inflammatory disease of the nasal mucosa induced by an immunoglobulin E-mediated reaction in subjects who are allergen sensitized. Although not life threatening, the symptoms of AR are frequently bothersome and adversely affect work and quality of life. In addition, AR implies elevated social costs and causes enormous socioeconomic burden.^{1–5} Accordingly, developing simple and effective treatment strategies is very important to stop its development.

China is the most populous country in the world. In recent years, with the rapid economic development and the great changes of lifestyle and social and natural environments, there is an increasing prevalence of AR. Two recent studies indicated that, despite variations in the prevalence of AR in different regions of the country, the prevalence of AR has increased in both adults and children over the past two decades.^{6,7} Given that house-dust mites were identified as the most common allergens in many regions of China,^{8–10} it is important to avoid exposure to dust-mite allergy to prevent and treat AR.

Dr. Theiss Alergol Pollen Blocker (hereafter called Pollen Blocker) (Dr. Theiss Naturwaren GmbH, Homburg, Germany) is a viscous topical nasal cream, and it contains highly purified aliphatic long-chain hydrocarbons of high quality. Pollen Blocker is a further, prop-

rietary, development of standard pharmaceutical petrolatum with a better spreadability. When applied to the lower nose region, it forms a mechanical barrier that prevents airborne allergens from contacting the mucous membrane of the nose, thereby relieving allergy symptoms. The ointment has already been distributed as a medical treatment among European countries due to its efficacy and low risk of adverse effects. Researchers have confirmed the efficacy of Pollen Blocker for patients with AR sensitized to pollen, house dust, and animal dander.^{11–15} However, the sample size in the previous studies was small, no multicenter randomized controlled trial was conducted in China, and the efficacy of this nasal ointment against dust-mite allergy was inconclusive. Consequently, the present study aimed to further clarify the efficacy and safety of Pollen Blocker against mite allergens in Chinese patients.

MATERIALS AND METHODS

Study Design

A multicenter, randomized, double-blind, placebo-controlled, crossover study was conducted from September to December 2011, in the outpatient clinics of the departments of otolaryngology at the Eye and ENT Hospital of Fudan University, the First Affiliated Hospital of Nanjing Medical University, the Traditional Chinese Medicine Hospital of Jiangsu Province, and the Second Affiliated Hospital of Zhejiang University. The study protocol was approved by the ethics committees of all four hospitals, and written informed consent was obtained from each patient (or from their guardians if the subject was <16 years old) before their participation in the trial.

First, a 7-day preliminary assessment phase was carried out to determine whether the candidates met the criteria for inclusion in the study. Patients ages 6 to 60 years and diagnosed with at least 1 year of perennial AR (confirmed by clinical history, positive skin-prick tests, and serum-specific immunoglobulin E of >0.7 kU/L), with an average total nasal symptom score (TNSS) of at least 20 during the week were included in the study. Exclusion criteria included known hypersensitivity to ingredients in the product under investigation, severe septum deviation, nasal pol-

From the ¹Department of Otolaryngology, the ENT Hospital, Fudan University, Shanghai, China, ²Department of Otolaryngology, the First Affiliated Hospital, Nanjing Medical University, Nanjing, China, ³Department of Otolaryngology, the Traditional Chinese Medicine Hospital of Jiangsu Province, Nanjing, China, and ⁴Department of Otolaryngology, the Second Affiliated Hospital, Zhejiang University, Hangzhou, China

Funded by the Action Plan 2014–2016 of Shanghai. Vital clinical project (ZY3-JSFC-1–1021) of traditional Chinese Medicine and integrated traditional Chinese and Western medicine

The authors have no conflicts of interest to declare pertaining to this article

Y. Li and L. Cheng contributed equally to this work

Address correspondence to Dehui Wang, M.D., Department of Otolaryngology, the ENT Hospital, Fudan University, 83 Fenyang Rd, Xuhui District, Shanghai, 200031
E-mail address: wangdehui1@sina.com

Copyright © 2015, OceanSide Publications, Inc., U.S.A.

Table 1 Comparison of population composition between groups 1 and 2

	Group 1, no. (%) (n = 57)*	Group 2, no. (%) (n = 58)†	χ^2	p Value‡
Sex				
Male	32 (56.1)	26 (44.8)	1.47	0.23
Female	25 (43.9)	32 (55.2)	0.07	0.78
Age				
16 y	13 (22.8)	12 (20.7)		
≥16	44 (77.2)	46 (79.3)		

*Received Pollen Blocker first then placebo.

†Received placebo first then Pollen Blocker.

‡p > 0.05.

yps, participation in other clinical trials within the preceding 30 days, concomitant disease that could affect the variables assessed in this study to such an extent that an objective judgment would not be possible, and women of childbearing age who are not using sufficient contraception.

After the 1-week lead-in period, the main phase of the study, which consisted of 30 days of treatment, was followed. In this period, eligible participants were randomized to receive the application of Pollen Blocker (5-g tube of ointment: a petrolatum-based ointment that contains highly refined long-chain hydrocarbons) or placebo (gel that contained 5% carboxymethylcellulose, 93.5% water, 0.5% citric acid, and 1% potassium sorbate). As stipulated on instruction, 1 cm of cream was applied with a cotton swab at a clean nasal vestibule of each nostril and spread evenly to the lower internal nose region three times daily. Each patient was requested to keep a record of application frequency in his or her diary.

From day 1 to 14, the patients applied Pollen Blocker or placebo. On day 14, a hospital visit was scheduled, and the patients returned their test product and did not use it after the visit. After 2 days of washout, day 17 marked the beginning of the second phase of treatment. The patients checked in and were issued the test product that they had not used in the first phase, in accordance with the crossover design schedule. The patients used the issued product from day 17 to day 30 in the same manner as they had applied the former product from day 1 to day 14. On day 30, the patients received a final examination.

Each patient was requested to keep a diary during the whole study period, logging the severity of nasal symptoms each day. The severity of individual nasal symptom (iNSS) (sneezing, nasal itching, rhinorrhea, and nasal congestion) was scored on a scale of 0 to 10 (visual analog scale), which grades the severity of symptoms from “no symptoms” (0 cm) to “the highest level of symptoms” (10 cm). In addition, the subjects were not allowed to use any antiallergy medications or drugs that could reduce AR during the entire study period. Adverse events (AE) were also monitored.

Statistical Analysis

The comparison between pre- and posttreatment values was performed by using the paired *t*-test and Wilcoxon signed rank test for normally and non-normally distributed data, respectively. The difference between the groups was analyzed by using the Student's *t*-test (for those with normal distribution) or the Mann-Whitney *U* test (for those with non-normal distribution). Mixed model analysis of variance for 2 × 2 crossover studies was fitted when assumption for normality was met. All analyses were performed with the Statistical Analysis Software (SAS, version 9.1; SAS Institute Inc., Cary, NC). A two-sided *p* value of <0.05 was considered statistically significant.

Table 2 Comparison between groups 1 and 2 before treatment

Characteristic	Group 1 (n = 57)		Group 2 (n = 58)		p Value*
	Mean (SD)	Min, max	Mean (SD)	Min, max	
Age, y	28.2 ± 14.6	7, 48	27.2 ± 14.0	6, 49	0.92
Duration, y	8.3 ± 5.7	2, 25	7.0 ± 5.1	1.5, 29	0.71
Rhinorrhea	6.1 ± 1.7	2, 10	6.3 ± 1.8	2, 10	0.74
Congestion	5.0 ± 2.1	0, 10	5.8 ± 2.3	1, 10	0.13
Itching	5.1 ± 2.2	0, 10	5.5 ± 2.0	1, 10	0.22
Sneezing	6.1 ± 1.8	1, 10	5.6 ± 2.1	0, 10	0.15
TNSS	20.8 ± 3.8	11, 33	21.7 ± 4.2	8, 40	0.31

Duration = duration of perennial AR; min = minimum; max = maximum; SD = standard deviation; TNSS = total nasal symptom score.

*p > 0.05.

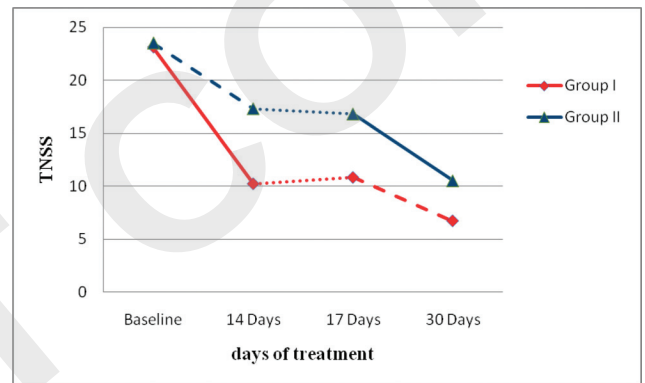


Figure 1. TNSS for the two groups at different follow-up visits. The solid line indicates Pollen Blocker, the dashed line is placebo, and the dotted line is the washout period.

RESULTS

Patient Population

A total of 120 patients with clinically proven perennial AR were recruited. Five of the patients did not fulfill inclusion requirements and were excluded; therefore, 115 subjects were included and randomized to treatment with Pollen Blocker or placebo. The sample was composed of 58 male and 57 female subjects: 25 children (<16 years of age) and 90 adults (≥16 years of age). The composition of patients at baseline was outlined in Tables 1 and 2. There was no significant difference between group 1 (first Pollen Blocker, then placebo) and group 2 (first placebo, then Pollen Blocker) for demographics, TNSS, and iNSS before treatment (*p* > 0.05). In addition to *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*, some frequent causative allergens, such as animal dander and pollen, were also tested. Regarding the percentage of allergens, all the subjects (*n* = 115) were sensitized to *D. farinae* and *D. pteronyssinus*, 46 to animal danders (40%), and 20 to pollen (17.4%).

Effect of Pollen Blocker Based on Crossover Design

Pollen Blocker was the product used by group 1 from day 1 to day 14 and was used by group 2 from day 17 to day 30. The mean values of TNSS for the two identical treatment phases are illustrated in Fig. 1. At baseline, there was no significant difference between the two groups (*p* > 0.05). On day 14, after treatment with the active nasal ointment, the TNSS of group 1 was significantly lower than that of group 2 (*p* < 0.001). After 2 days of washout, no great changes of TNSS had taken place. However, on day 30, after application of Pollen

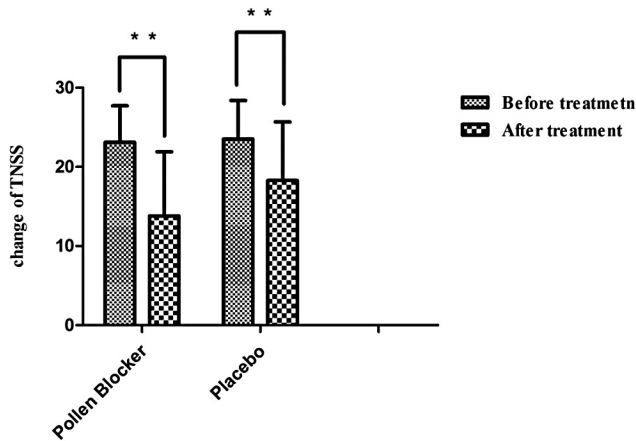


Figure 2. Change of TNSS between the Pollen Blocker group and the placebo group. Bars indicate the mean values of TNSS; brackets represent standard deviations. Paired *t*-test, ***p* < 0.001.

Table 3 Changes of allergy symptom scores after treatment

Symptom	Group	AT–BT	<i>p</i> Value*
TNSS	Pollen Blocker	−9.3 ± 7.0	<0.001
	Placebo	−5.2 ± 6.0	
Rhinorrhea	Pollen Blocker	−2.3 ± 2.5	0.004
	Placebo	−1.4 ± 2.4	
Congestion	Pollen Blocker	−2.1 ± 2.4	0.005
	Placebo	−1.3 ± 2.1	
Sneezing	Pollen Blocker	−2.6 ± 2.3	<0.001
	Placebo	−1.3 ± 2.2	
Itching	Pollen Blocker	−2.3 ± 2.2	<0.001
	Placebo	−1.3 ± 1.9	

AT–BT = subtract after treatment scores from before treatment scores; TNSS = total nasal symptom score.

**p* < 0.05, independent *t*-test.

Blocker, the TNSS of group 2 had significantly decreased (*p* < 0.001). Although the score of group 1 was lower than that of group 2, the decrease of group 2 (6.3) in the second stage was significantly higher than that of group 1 (4.1; *p* < 0.05). In summary, study results based on crossover design implied remarkable efficacy on TNSS of Pollen Blocker.

Efficacy of Pollen Blocker and Placebo

After completing the trial, we categorized all the data into the Pollen Blocker group and the placebo group. Then, the following results were obtained by group method of data handling. As shown in Fig. 2, after application of Pollen Blocker, the mean TNSS decreased from 23.1 to 13.8 points. Meanwhile, the TNSS of the placebo group fell from 23.5 to 18.3. Therefore, both Pollen Blocker and placebo led to a significant decrease in TNSS in comparison with the start value on day 0 (*p* < 0.001, paired *t*-test). However, the decrease in TNSS of the Pollen Blocker group (9.3) was highly significant compared with the placebo group (5.2) (*p* < .001). Similarly, the decreases in iNSS (rhinorrhea, congestion, sneezing, and itching) between Pollen Blocker group and the placebo group were also significant (*p* < 0.05, independent *t*-test). As Table 3 shows, the Pollen Blocker was significantly more effective than placebo.

In addition, the sample was composed of 90 adults (≥16 years old) and 25 children (<16 years). In adults, Pollen Blocker led to a remarkably significant decrease in TNSS (9.5) compared with the placebo (5.4; *p* < 0.001); in children, the pollen blocker led to a

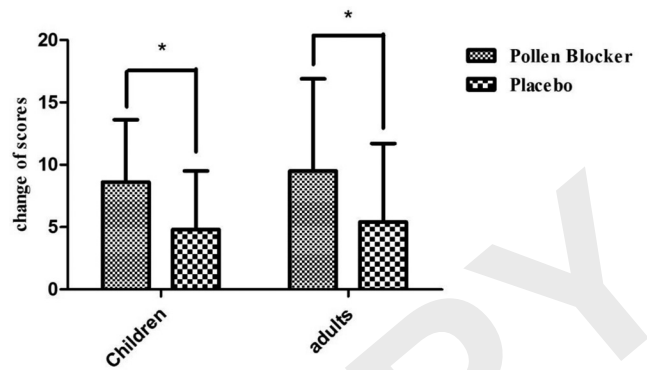


Figure 3. Change of TNSS in both children and adults. Bars indicate the mean values; brackets represent standard deviations. **p* < 0.05, independent *t*-test.

Table 4 Cross-analysis of the decrease in total nasal symptom score

Source	F value	<i>p</i> Value
Sequence	0.00	0.99
Period	0.17	0.68
Ptid (seq)	0.73	0.91
Treatment (Pollen Blocker)	25.34	<0.001**

Ptid (seq) = nested effect.

***p* < 0.001.

Table 5 AEs that occurred in Pollen Blocker and placebo groups

AEs	Pollen Blocker Group (n = 3)	Placebo Group (n = 2)	<i>p</i> Value
Rhinorrhea	1	1	1
Nasal congestion	1		
Epistaxis	1		
Burning sensation		1	

significant decrease in TNSS (8.6) compared with placebo (4.8; *p* < 0.05). As Fig. 3 shows, the efficacy of Pollen Blocker was significantly more effective than the placebo in both adults and children. Also, the study was designed as a crossover trial, which can eliminate the effects of nontrial factors as much as possible. As manifested in Table 4, after controlling of the sequence, period, and nested effect of subjects, the efficacy of Pollen Blocker was also significant (*p* < 0.001).

AEs

Five subjects underwent mild AEs: three in the Pollen Blocker group (2.5%) and two in the placebo group (1.7%) for which they did not need to be on any medication. There was no significant difference in the incidence of AEs between the Pollen Blocker group and the placebo group (*p* > 0.05). As shown in Table 5, rhinorrhea, nasal congestion, epistaxis, and burning sensation in the anterior nasal were commonly reported. No severe systemic reactions were observed.

DISCUSSION

AR is a global health problem, and its incidence and prevalence are increasing in China and around the world. Allergy symptoms can lead to both physical and mental complications, with sleep-disordered breathing in childhood and adolescence being associated with decreased learning performance and increased behavior and attention

disorders.^{16–19} In addition, AR has a major negative impact on national and global health economics due to direct and indirect costs.^{20,21} Because 20% of people with rhinitis are not helped by guideline-directed pharmacotherapy,²² more effective and convenient treatments should be sought and popularized.

Allergen avoidance is viewed as a causal treatment strategy for AR. However, it is hard to avoid airborne allergens completely. Fortunately, with the advance of medical devices and the emergence of a new product, nose ointment could be a suitable alternative remedy to avoid or reduce the inhalation of allergens. The investigational product Pollen Blocker is a new petrolatum-based ointment that contains highly refined long-chain hydrocarbons and has a property of high affinity and high viscosity for particulate matter, such as dust-mite allergy and other allergens.²³ Pollen Blocker is highly viscous and nonabsorbent; when applied to the lower nose region, it forms a mechanical barrier that entraps aeroallergens and reduces the number of allergens that enter the nose, thereby relieving allergy symptoms.

The efficacy of petrolatum-based ointment has been confirmed in several studies. Bufo,¹¹ who only tested pollen in his study, observed that intranasal application of a petrolatum-based ointment effectively relieved the symptoms of AR in 15 patients during the pollen season, which implies that the mechanism was equivalent to allergen avoidance. In another study,⁷ a highly purified, highly viscous nose ointment with a petrolatum base achieved a significant decrease in allergic symptom score, without causing AEs.¹² In 2004, Schwetz *et al.*¹³ used a nasal provocation test to demonstrate that the ointment that was the same as our product was significantly more effective than placebo in reducing allergy symptoms. In 2005, a study that included 33 patients with AR showed that the lipid-based nose ointment tested here led to a significant improvement in sneezing and nasal itching (17 patients), and, meanwhile, all the scores remained unchanged in the untreated control group (16 patients).¹⁴ A recently published study in 2013 demonstrated that the Pollen Blocker was significantly more effective than placebo in relieving nasal allergy symptom and improving quality of life in 30 Chinese people.¹⁵ These findings provide further evidence in favor of the efficacy of nose ointment against aeroallergens.

As mentioned above, the efficacy of Pollen Blocker was encouraging. However, the sample size in the previous studies was small, and to our knowledge no multicenter, randomized controlled trial in China has clearly demonstrated the efficacy of this product against dust-mite allergy. In this multicenter, randomized, double-blind, placebo-controlled, crossover study, which included 115 patients with mite-induced AR, we observed that the efficacy of Pollen Blocker ointment was significantly more effective than placebo, which manifested in both TNSS and iNSS. Statistical analysis based on a crossover study also verified the case. Furthermore, the results demonstrated that the efficacy of Pollen Blocker was superior to placebo, both in adults and children, which indicated that the efficacy of this nasal ointment had no relation to age. In addition, multiple sensitization is common in patients with AR⁸: in our study, 17 patients (14.8%) were monosensitized to *D. pteronyssinus* and *D. farinae*, and 98 subjects (85.2%) were concomitantly sensitized to relevant allergens (animal dander or pollen), which is consistent with other studies,^{24–26} and confirmed that dust mites are the most important source of aeroallergens. Of note, our study supplies further evidence in favor of the efficacy of Pollen Blocker against dust-mite allergy.

A strong placebo effect has been observed in allergy trials.²⁷ In our study, we also observed the similar placebo effect as presented by Schwetz *et al.*¹³ and Li *et al.*¹⁵: the placebo group also had a reduction of nasal symptoms in TNSS compared with the start value. On one hand, the carboxymethylcellulose control substance is not a real placebo but rather a comparator product. The fact that even the placebo gel has a certain effect in trapping allergens confirms the appropriateness of the barrier principle of Pollen Blocker. On the other hand, the placebo could not have the same effect as the active treatment due

to its composition characteristics. Our study results also verified the case: all data based on statistical analysis showed that the efficacy of Pollen Blocker was superior to placebo.

Concerning the safety of nose ointment, health hazards arise only as a result of the ointment's physical effects on the gastrointestinal tract or airways when accidentally swallowed or aspirated.¹³ For now, only one case of petrolatum-induced pneumonia has been documented in one patient.²⁸ As for the Pollen Blocker, it is a mixture of high purity, of long-chain hydrocarbons in a high-viscosity mineral oil base, which is not metabolized and hypoallergenic. In our study, the ointment did not produce any severe AEs, and the incidence of AEs (such as mild rhinorrhea, nasal congestion, epistaxis and burning sensation) between the Pollen Blocker group and the placebo group was not significantly different. Consequently, the Pollen Blocker is proved to be safe and well tolerated.

Although AR is not a serious illness, it is clinically relevant and affects quality of life and productivity at work or school.²² In the first multicenter, randomized, placebo-controlled, crossover study of evaluating the efficacy of Pollen Blocker against dust-mite allergy, we demonstrated that the petrolatum-based ointment is significantly more effective than the placebo in relieving TNSS and iNSS in both adults and children. Based on the study, we concluded that Pollen Blocker ointment is a safe and effective alternative to the drugs for treatment of AR, especially for Chinese patients sensitive to dust-mite allergen. In addition, our results can provide some evidence because changes in the therapeutic guidelines may be suggested in the future.

REFERENCES

1. Canonica GW, Bousquet J, Mullol J, et al. A survey of the burden of allergic rhinitis in Europe. *Allergy* 62(suppl. 85):17–25, 2007.
2. Bellanti JA, and Settipane RA. The burden of allergic rhinitis on patients' quality of life. *Allergy Asthma Proc* 33(suppl. 1):S112, 2012.
3. Benninger MS, and Benninger RM. The impact of allergic rhinitis on sexual activity, sleep, and fatigue. *Allergy Asthma Proc* 30:358–365, 2009.
4. de la Hoz Caballer B, Rodríguez M, Fraj J, et al. Allergic rhinitis and its impact on work productivity in primary care practice and a comparison with other common diseases: The Cross-sectional study to evaluate work Productivity in allergic Rhinitis compared with other common diseases (CAPRI) study. *Am J Rhinol Allergy* 26:390–394, 2012.
5. Meltzer EO, Blaiss MS, Naclerio RM, et al. Burden of allergic rhinitis: Allergies in America, Latin America, and Asia-Pacific adult surveys. *Allergy Asthma Proc* 33(suppl. 1):S113–S141, 2012.
6. Zhang Y, and Zhang L. Prevalence of allergic rhinitis in China. *Allergy Asthma Immunol Res* 6:105–113, 2014.
7. Song N, Shamssain M, Mohammed S, et al. Prevalence, severity and risk factors of asthma, rhinitis and eczema in a large group of Chinese schoolchildren. *J Asthma* 51:232–242, 2014.
8. Li J, Sun B, Huang Y, et al. A multicentre study assessing the prevalence of sensitizations in patients with asthma and/or rhinitis in China. *Allergy* 64:1083–1092, 2009.
9. Sun JL, Shen L, Chen J, et al. Species diversity of house dust mites in Beijing, China. *J Med Entomol* 50:31–36, 2013.
10. Chen JJ, Kong WJ, Xiang JS, et al. Analysis of age characteristics of allergen in HUBEI area. *J Clin Otolaryngol Head Neck Surg* 22:683–685, 2008.
11. Bufo A. A simple advice for the prevention of pollen-induced allergic rhinitis. *Int Arch Allergy Immunol* 121:85–86, 2000.
12. Olze H, Wustrow TPU, and Grigorov A. Provokationstest mit Immerfit Pollenschutzcreme bei Patienten mit allergischer Rhinitis. *Erfahrungsheilkunde (Heidelb)* 51:416–421, 2002.
13. Schwetz S, Olze H, Melchisedech S, et al. Efficacy of pollen blocker cream in the treatment of allergic rhinitis. *Arch Otolaryngol Head Neck Surg* 130:979–984, 2004.
14. Geisthoff UW, Blum A, Rupp-Classen M, et al. Lipid-based nose ointment for allergic rhinitis. *Otolaryngol Head Neck Surg* 133:754–761, 2005.

15. Li Y, Wang D, Liu Q, et al. Randomized double-blind placebo-controlled crossover study of efficacy of pollen blocker cream for perennial allergic rhinitis. *Am J Rhinol Allergy* 27:299–303, 2013.
16. Nathan RA. The burden of allergic rhinitis. *Allergy Asthma Proc* 28:3–9, 2007.
17. Blaiss MS. Pediatric allergic rhinitis: Physical and mental complications. *Allergy Asthma Proc* 29:1–6, 2008.
18. Lv X, Han D, Xi L, and Zhang L. Psychological aspects of female patients with moderate-to-severe persistent allergic rhinitis. *ORL J Otorhinolaryngol Relat Spec* 72:235–241, 2010.
19. Xi L, Zhang Y, Han D, and Zhang L. Effect of asthma, aeroallergen category, and gender on the psychological status of patients with allergic rhinitis. *J Investig Allergol Clin Immunol* 22:264–269, 2012.
20. Blaiss MS. Allergic rhinitis: Direct and indirect costs. *Allergy Asthma Proc* 31:375–380, 2010.
21. Akdis C, Papadopoulos N, and Cardona V. Fighting allergies beyond symptoms: The European Declaration on Immunotherapy. *Eur J Immunol* 41:2802–2804, 2011.
22. Greiner AN, Hellings PW, Rotiroti G, et al. Allergic rhinitis. *Lancet* 378:2112–2122, 2011.
23. Shah R, and Grammer LC. Chapter 1: An overview of allergens. *Allergy Asthma Proc* 33(suppl. 1):S2–S5, 2012.
24. Squillace SP, Sporik RB, Rakes G, et al. Sensitization to dust mites as a dominant risk factor for asthma among adolescents living in central Virginia. Multiple regression analysis of a population-based study. *Am J Respir Crit Care Med* 156:1760–1764, 1997.
25. Leung R, and Jenkins M. Asthma, allergy and atopy in southern Chinese school students. *Clin Exp Allergy* 24:353–358, 1994.
26. Yasueda H, Mita H, Yui Y, and Shida T. Comparative analysis of physicochemical and immunochemical properties of the two major allergens from *Dermatophagoides pteronyssinus* and the corresponding allergens from *Dermatophagoides farinae*. *Int Arch Allergy Appl Immunol* 88:402–407, 1989.
27. del Cuvillo A, Sastre J, Bartra J, et al. Placebo effect in clinical trials involving patients with allergic rhinitis. *J Investig Allergol Clin Immunol* 21(suppl. 3): 40–45, 2011.
28. Brown AC, Slocum PC, Putthoff SL, et al. Exogenous lipid pneumonia due to nasal application of petroleum jelly. *Chest* 105:968–969, 1994. □

Copyright of American Journal of Rhinology & Allergy is the property of OceanSide Publications Inc. and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.