

## การศึกษาถึงความสำคัญของสารก่อภูมิแพ้ในเด็กที่ป่วยเป็นโรคภูมิแพ้จมูกอักเสบจากภาคตะวันออกของประเทศไทย

เบญจรัตน์ ทรรทรานนท์(พ.บ.) ทวีลาภ ตันสวัสดิ์ (พ.บ.) และปราการ ทัดติยกุล (พ.บ.)

สาขาวิชากุมารเวชศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยบูรพา ชลบุรี ประเทศไทย

### บทคัดย่อ

**บริบท** อุบัติการณ์โรคภูมิแพ้จมูกอักเสบสูงขึ้นทั่วโลกรวมทั้งประเทศไทยสารก่อภูมิแพ้เป็นปัจจัยสำคัญในการเกิดโรค ข้อมูลการแพ้สารก่อภูมิแพ้ในอากาศภาคตะวันออกของประเทศไทยยังมีไม่มากจึงเป็นที่มาของการศึกษา **วัตถุประสงค์** ศึกษาการแพ้สารก่อภูมิแพ้ในผู้ป่วยเด็กโรคเยื่อจมูกอักเสบจากภูมิแพ้ โรงพยาบาลมหาวิทยาลัยบูรพาย้อนหลัง 5 ปีตั้งแต่ พ.ศ.2559-2563

**วิธีการศึกษา** ศึกษาย้อนหลังเชิงพรรณนา ในผู้ป่วยเด็กโรคภูมิแพ้จมูกอักเสบอายุ 2-15 ปี 100 ราย ที่คลินิกโรคภูมิแพ้โรงพยาบาลมหาวิทยาลัยบูรพา เก็บข้อมูลพื้นฐาน ตัวโรควิเคราะห์ข้อมูลด้วยสถิติเชิงพรรณนา Chi-square tests และ and Fisher's exact tests

**ผลการศึกษา** อายุเฉลี่ย  $9.63 \pm 3.14$  ปี สารก่อภูมิแพ้ที่ให้ผลบวกมากที่สุด 3 ลำดับแรก ได้แก่ Dermatophagoides pteronyssinus (Dp) (ร้อยละ 90) รองลงมา D. Farinae (ร้อยละ 68) และ American cockroach (ร้อยละ 33) ส่วนสารก่อภูมิแพ้อื่นๆ German cockroach, Cat dander, Bermuda, Careless weed, Dog dander, Acacia, Aspergillus, Cladosporium, Alternaria, Johnson grass, Para grass พบร้อยละ 23, 16, 13, 13, 12, 12, 12, 11, 8, 7 และ 7 ตามลำดับ ผู้ป่วยที่แพ้สารก่อภูมิแพ้มากกว่า 1 ชนิด พบโรคร่วมมากกว่ากลุ่มที่แพ้เพียง 1 ชนิด 1.92 เท่า แต่ไม่พบความแตกต่างอย่างมีนัยสำคัญ (ร้อยละ 52.17 และ ร้อยละ 35.48, OR 1.92, 95% CI 0.80-4.63,  $p = 0.14$ ) ผู้ป่วยที่มีโรคร่วมเยื่อตาอักเสบจากภูมิแพ้ แพ้ไรฝุ่นมากที่สุด (ร้อยละ 96.55) การประเมินความรุนแรงของโรคตาม ARIA classification พบ mild persistent AR มากที่สุด (ร้อยละ 86) ทุกคนในกลุ่ม moderate-severe persistent AR ใช้น้ำยาเดี่ยวรอยด้นจมูกอย่างสม่ำเสมอเมื่อเทียบกับกลุ่มที่รุนแรงน้อยกว่า (ร้อยละ 100 และ ร้อยละ 51.7,  $p = 0.03$ ), กลุ่ม mild intermittent AR มีอัตราการหายจากโรคสูงกว่ากลุ่ม moderate-severe persistent AR (ร้อยละ 100 และ ร้อยละ 14.3,  $p = 0.003$ ) อย่างมีนัยสำคัญ

**สรุป** ไรฝุ่นเป็นสารก่อภูมิแพ้ที่พบมากที่สุดในผู้ป่วยเด็กโรคภูมิแพ้จมูกอักเสบในภาคตะวันออกของประเทศไทย คล้ายกับการศึกษาที่ผ่านมาในภูมิภาคอื่นในประเทศ พบการแพ้สารก่อภูมิแพ้นอกบ้านมากกว่าการศึกษาที่ผ่านมา (grasses, weeds, molds เช่น Cladosporium และ Alternaria) พบการแพ้รังแคแมวและรังแคสุนัขมากขึ้น

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**ผู้พิมพ์ที่รับผิดชอบ**

เบญจรัตน์ ทรธรานนท์

สาขาวิชากุมารเวชศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยบูรพา

จังหวัดชลบุรี ประเทศไทย

E-mail: benzjarut@hotmail.com

## Patterns of aeroallergen sensitization among children with allergic rhinitis in eastern Thailand

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Benjarat Dardaranonda (M.D.), Taweelarp Tansavatdi (M.D), Prakarn Tattiyakul (M.D.)

Department of Pediatrics, Faculty of Medicine, Burapha University, Chonburi, Thailand

### Abstract

**Introduction:** Allergic rhinitis (AR) is the most common chronic disease among children in Thailand as well as in other parts of the world. Knowledge about the patterns of allergen sensitization among these children is important since it will lead to a better understanding of the disease's pathogenesis, prevention and treatment. Currently, there is a limitation of data on allergy sensitization among these children in Eastern Thailand.

**Objective:** To study a 5-year pattern of allergen sensitization among children with AR presenting to the Pediatric Allergy Clinic of the Burapha University Hospital. The 5-year period was from 2016 to 2020.

**Materials and methods:** A retrospective and descriptive study of 100 children with AR, aged 2-15 years, was conducted at the Pediatric Allergy Clinic of the Burapha University Hospital. Demographic and clinical data were collected and analyzed with an SPSS statistical package using appropriate descriptive and comparative modules.

**Results:** The mean age (SD) of the subjects in this study was 9.63 (3.14) years. The third most common cause of allergy sensitization in this group of patients was *Dermatophagoides pteronyssinus* (Dp)(90%), followed by *Dermatophagoides farinae* (Df) (68%) and American cockroaches (33%). Other allergens included German cockroaches, cat dander, Bermuda grass, careless weed, dog dander, acacia, *Aspergillus*, *Cladosporium*, *Alternaria*, Johnson grass, and Para grass at 23, 16, 13, 13, 12, 12, 12, 11, 8, 7, and 7% respectively. Children sensitized to a greater number of allergens were not significantly associated with increased risk of other comorbidities (52.17% vs 35.48%, OR 1.92, CI 0.80-4.63,  $p = 0.14$ ). Children with allergic conjunctivitis in addition to rhinitis were found to be mite-sensitized by 96.5%. As per Allergic Rhinitis as Initiative for Asthma (ARIA) classification, 86% had mild-persistent AR. All patients with moderate-to-severe AR regularly used intranasal corticosteroids – which was significantly more frequently used than those with less severity (100% vs 51.7%,  $p = 0.03$ ). Those with mild-intermittent AR had a higher remission rate as compared with those having moderate and severe AR (100% vs 14.3%,  $p = 0.003$ ).

**Conclusion:** Similar to studies from other parts of Thailand, house dust mites are the most common causes of AR among children in eastern Thailand. Slightly higher sensitization to outdoor allergens (grasses, weeds and molds such as Cladosporium and Alternaria) was also observed. This is perhaps due to a higher rate of exposure to these outdoor allergens. A higher sensitization to cat and dog dander was also noted.

**Keywords:** Allergic rhinitis, Children, Aeroallergens, Dust mites, Grasses, Cats, Dogs

**Corresponding author:** Benjarat Dardaranonda  
Department of Pediatrics, Faculty of Medicine  
Burapha University, Chonburi, Thailand  
E-mail: benzjarut@hotmail.com

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## Introduction

Over the past 30 years, there has been an increasing prevalence of allergic rhinitis (AR) all over the world.<sup>1,2</sup> Previously, the global percentage of AR prevalence was estimated to be around 10-25%.<sup>3</sup> However, recent reports have indicated that prevalence of AR in the Asia-Pacific alone has increased from 37.9% to 50% of the population.<sup>4</sup> Such an increase has had a significant economic effect on the country's healthcare, both directly and indirectly.<sup>1,2</sup> Understanding the prevalence of allergy sensitization among AR patients inside each region of Thailand is important since it will lead to a better implementation of environmental control towards specific allergens, inside and outside, and thus lead to an improved state of medical care.<sup>5,6</sup> A starting point is to observe differences in common allergens among various countries. For example, while house dust mites are important for the tropics and subtropical climates such as in Asia and South America<sup>7</sup>, the more temperate climate areas such as the USA and Europe are faced with outdoor allergens such as grass and tree pollens.<sup>8</sup> Moreover, pet danders such as cat and dog have become one of the leading allergens for Scandinavians such as in Sweden and Norway.<sup>9</sup>

There have been several studies on the prevalence of allergen sensitization performed from the three main regions in Thailand (the central region of Bangkok and Nonthaburi, the northern region of Chiang Mai and the northeastern region of Surin).

Most of these studies indicated that house dust mites were the most important allergens sensitized by allergic Thai children (60.7% to 92%). *Dermatophagoides pteronyssinus* (Dp), a species of HDM requiring higher humidification for survival, was the most common sensitizer (up to 90%), followed by *D. farinae* (requiring lower humidity) at around 60%. American and German cockroaches were the second group of allergens causing sensitization (30-40%). The prevalence of outdoor allergens such as grasses, trees, and molds are less common than indoor allergens. Furthermore, none of these studies were conducted on children or adults residing along the seacoast of eastern Thailand, which has a different climate and ecological system, compared with other parts of the country. Therefore, it is important that this information be used to manage children with allergies living in the inland eastern part of the country, and thus form the intended subjects for the current report.

## Objective

To study a 5-year pattern of allergen sensitization among children with AR presenting to the Pediatric Allergy Clinic of the Burapha University Hospital from 2016-2020.

## Materials and Methods

We retrospectively collected data from the medical records of 100 children aged 2-15 years, who were diagnosed as having symptoms of allergic rhinitis (AR) between January 2019 and December 2020. We further screened for diagnoses made by well-trained

pediatric allergists at least 6 months prior to visiting us at the Pediatric Allergic Clinic of the Department of Pediatrics at Burapha University Hospital. The criteria for the diagnosis of AR included a classic history of AR symptoms (nasal congestion and blockage, sneezing, itching and watery rhinorrhea), and a positive allergy skin prick test to one or more allergens (having a wheal size greater than the positive histamine control).<sup>17-19</sup> Skin prick tests were performed using common aeroallergen skin test extract reagents for Thailand (ALK®, Port Washington, NY). The Research Ethics Committee of Burapha University, Chonburi, Thailand, approved this study (1-016/2564).

Collected data included the patient's age, sex, age at the onset of allergic rhinitis, other atopic diseases, family history of atopic diseases, skin prick test results, current medications and drug compliance. Diagnosis of other atopic diseases were made by an attending allergist. AR was classified using ARIA classification (Allergic Rhinitis and its Impact on Asthma<sup>3</sup>) as being either mild-intermittent, moderate-severe intermittent, mild-persistent, and moderate-severe persistent. 'Intermittent' was defined as symptoms having occurred <4 days per week or <4 consecutive weeks. 'Persistent' was classified when symptoms occurred >4 days/week and >4 consecutive weeks. Symptoms were considered mild with normal sleep, no impairment of daily activities and no impairment to work or school. Severe symptoms resulted in sleep disturbance, impairment of daily activities and an impairment to work or school.

## Assessments

**Statistical Analyses** All analysis were performed with the IBM SPSS ver. 27.0 (IBM Co., Armonk, NY, USA). Descriptive statistics were used for the characteristics and sensitization patterns among enrolled patients. Chi-square tests and Fisher's exact tests were used to compare proportions of the patients' characteristics including types of aeroallergen sensitization (e.g., monosensitization vs polysensitization or indoor allergen vs outdoor allergen), frequency of intranasal corticosteroid use and any remission of allergic rhinitis among the 4 classified groups. An odds ratio with a 95% confidence interval was calculated to determine the graded effect of numbers of aeroallergen reactivities with a risk of coexistence of allergic rhinitis and a risk of having house dust mite sensitization.

## Results

Among the 100 enrolled patients, 67 were male and 33 were female. The mean age  $\pm$  SD was  $9.63 \pm 3.14$  years. Table 1 shows the demographic data of these patients. The mean age at the diagnosis of AR was  $4.67 \pm 2.63$  years. The associated allergic diseases were allergic conjunctivitis (29%), atopic dermatitis (28%) and asthma (21%). The percent of patients with a family history of allergic diseases was 69%. Most patients indicated their disease severity in the mild-persistent class (86%). 36% of the patient's houses reported pets. 16% of the patient's houses reported smoking.

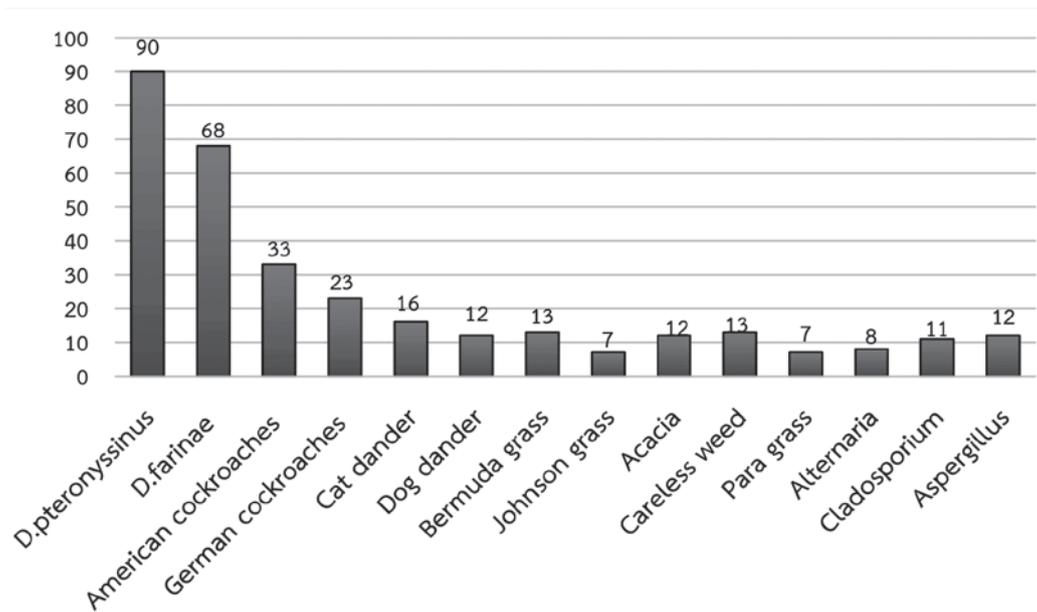
**Table1** Characteristics of patients with allergic rhinitis (n=100)

Demographic characteristics	n = 100
Sex	
Male	67
Female	33
Age (Years)	
Mean±SD	9.63 ± 3.14
Minimum-maximum	3.60 - 15
Mean age at diagnosis of AR	4.67 ± 2.63
Family history of allergic diseases	67
Associated allergic diseases	69
Allergic conjunctivitis	29
Atopic dermatitis	28
Asthma	
ARIA classification* of severity of AR	21
Mild intermittent symptoms	7
Mild persistent symptoms	86
Moderate to severe persistent symptoms	7
Home environment	
Owning dogs	21
Owning cats	6
Owning dogs and cats	10
No pets	63
Passive smoking exposure	16

**Note:** \*ARIA classification (Allergic rhinitis and its Impact on Asthma)

Figure 1 shows the frequency distribution of positive skin testing to various allergens. Sensitization to indoor allergens was observed more frequently than to outdoor allergens (99 vs 23 patients). House dust mites (Dp and Df) were the most frequent sensitized allergens (90% and 68% respectively), followed by American cockroaches (33%) and German cockroaches (23%). Cat allergy sensitization (16%) was more common than dog (12%). Sensitization to outdoor allergens

ranged from 7% (Johnson grass) to 13% (Bermuda grass). 53 patients were sensitized to only one allergen (monosensitization), while 46 were polysensitized. The degree of AR severity between monosensitization vs polysensitization was not statistically significant (85% vs 82%.  $P > 0.05$ ). Furthermore, while the polysensitized group typically had higher frequencies of associated allergic diseases over the monosensitized group (52% vs 48%), there was no statistical difference observed between the two groups ( $p > 0.05$ ).



**Figure 1** Frequency distribution of positive skin testing to various allergens D. pteronyssinus = Dermatophagoides pteronyssinus; D. farinae = Dermatophagoides farina

Although patients with moderate-severe persistent AR appeared to have more associated allergic diseases, the difference from those without other diseases was not statistically significant ( $p > 0.05$ ) (Table 2).

Intranasal steroids were used more frequently among those with more severe diseases (100% vs 51.5%,  $p = 0.03$ ). Remission among patients within the mild-persistent category was higher than among those with more severe diseases (52.3 vs 14.3%,  $p = 0.003$ )

**Table 2** Overview of the ARIA classification across the presence of associated allergic diseases, the use of intranasal steroids and remission from allergic rhinitis

ARIA classification†	Mild-intermittent n (%)	Mild-persistent n (%)	Moderate-severe persistent n (%)	p value†
Presence of associated allergic diseases				
Yes	5 (71.4)	60 (69.8)	4 (57.1)	0.89
No	2 (28.6)	26 (30.2)	3 (42.9)	
Use of intranasal steroids				
Regular use	-	30 (51.7)	7 (100)	0.03*
On demand use	-	28 (48.3)	0 (0)	
Remission from allergic rhinitis				
Remission	7 (100)	45 (52.3)	1 (14.3)	0.003*
No remission	0 (0)	41 (47.7)	6 (85.7)	

**Note:** †Fisher's Exact Test

As indicated in Table 3, AR patients with associated allergic conjunctivitis had a higher positive SPT rate to HDM than those without (96.5%). Similarly, AR with AD and with AS had a high positive SPT rate to HDM (96.4% and 90.48%, respectively). Among those with conjunctivitis, the rate of HDM positivity was 3 times higher than those without AC (OR = 3.06, CI 0.36-26.07,  $p = 0.43$ ). Odd ratios and CI for those with AD and with AS were 2.9, 95% CI = 0.34-24.78,  $p = 0.44$  and 0.78, CI 0.15-4.18,  $p = 0.67$ , respectively.

**Table 3** HDM sensitization and the presence of associated allergic diseases

AR with comorbidities	HDM sensitization (%)	Odd ratio Vs those without associated disease	95% CI	p-value*
AR with AC	96.55	3.06	0.36-26.07	0.43
AR with AD	96.43	2.90	0.34-24.78	0.44
AR with Asthma	90.48	0.78	0.15-4.18	0.67

**Note:** \*Fisher's Exact Test; AR : Allergic rhinitis; AC : Allergic conjunctivitis; AD : Atopic dermatitis, HDM : House dust mite

**Table 4** Prevalence of allergen sensitization among allergic children and adults from previous studies plus our current study

Age (yr)	Site, Year	HDM (%)			Cockroach (%)			Pet (%)			Grass (%)		
		Dp	Df	Mixed mites	Am CR	Ger CR	Mixed	Cat	Dog	Bermuda grass	Johnson grass	Mixed grasses	Others (%)
10-59	Pramongkutklo Hospital, 1997 <sup>10</sup>	76	79	-	60	41	-	29	28	17	21	-	9-30
0-16	Siriraj Hospital, 1997 <sup>11</sup>	67	62	-	44	-	-	10	5	-	14	-	2-7
6-15	Chulalongkorn University Hospital, 1998 <sup>12</sup>	-	-	92.13	-	-	53.77	27.87	13.7	-	-	53.11	34.09-89.18
0-15	Chiang Mai University Hospital, 2000 <sup>13</sup>	77.1	-	-	-	-	-	38.10	-	-	-	6.70	-
3-15	Thammasat university Hospital, 2004 <sup>14</sup>	79	69	-	30	20	-	13	8	16	15	-	8-29
1-15	Surin Hospital, 2011 <sup>15</sup>	60.7	56.6	-	-	-	47.4	18.5	7.5	30.1	37	-	4.6
7-90	Ramathibodi Hospital, 2018 <sup>16</sup>	-	-	64.8	-	-	32.3	12.9	10	-	-	36	1.5-4
2-15	Burapha University Hospital, 2021	90	68	-	33	23	-	16	12	13	7	-	7-13

**Note:** Dp = Dermatophagoides pteronyssinus, Df = Dermatophagoides farina, Am CR = American cockroach, Ger CR = German cockroach

## Discussion

Our data on allergy skin prick testing among Thai children from Eastern Thailand completes a general picture on the pattern of allergen sensitization in Thailand. Previously, there have been 7 similar studies conducted in Thailand<sup>10-16</sup> (5 from Bangkok and its vicinities<sup>10-12,14,16</sup>, 1 from Chiangmai<sup>13</sup> and 1 from the province of Surin).<sup>15</sup> In addition this study, 6 of the previous studies included children up to 15 years of age, while 2 of the studies included both children as well as adults (Table 4). It is quite clear from all studies that indoor allergens (house dust mites, cockroaches, and pets) are more important than outdoor allergens (grass and outdoor molds) for the Thais. House dust mites were the most common allergens found responsible for sensitization in the 8 total studies (with a range from 60-90% of the subjects) with roughly an equal degree of sensitization between Dp and Df. Of all the 8 studies, frequency of sensitization to dust mites were highest in our study (90%), perhaps due to the fact of an all year high humidity and high temperature in eastern Thailand – a favorable breeding ground for dust mites. Sensitization to cockroaches occurred between 30-40% across all studies<sup>11-16</sup> with the exception of a very high rate from the Pramongkutklao Hospital study from 1997 (60%).<sup>10</sup> There is a tendency for the American cockroach to be more important than the German cockroach. Sensitization to cat dander also differed between the studies, with the most showing

a sensitization rate to be about 15%. Studies which showed high sensitivity rates to cats were from Chulalongkorn Hospital<sup>12</sup> (27.8%) and Chiangmai Hospital<sup>13</sup> (38%). Cats were reported to be a major allergen for children in Scandinavia, possibly due to the necessity to keep cats indoors due to the low outside temperature<sup>9</sup>. With the increased popularity of keeping pets in the house, cats and dogs have emerged as major allergens for the Thais as well.

As for outdoor allergens, grass was responsible for approximately a 15% sensitization rate among most studies (including this study). The highest grass sensitization rate (38%) came from Surin<sup>15</sup> province where exposure to grass was probably more intense. Surprisingly, the rate of grass sensitization in our study is similar to those reported from central Bangkok,<sup>10-12,14,16</sup> indicating that eastern Thailand is becoming more urbanized with less grass prevailing in this part of Thailand, as compared to the northeastern part of the country.

Disease severity among most of our patients was highest in the mild-persistent group (86%). This is in contrast to results from the study by Chinratanapisit,<sup>20</sup> in which the percentage of the severe group was only 1.5%. In our study, a high rate of intranasal corticosteroid use among the persistent group (i.e., 100%) supports severity grading among our patients. Polysensitization was related to the presence of associated allergic diseases in this study. This reaffirms the findings from

Sritipsuko<sup>14</sup> among 3-15 year-old subjects (from 122 patients), that the number of positive skin tests was related to the presence of allergic comorbidities. We also demonstrated that allergic comorbidities affected the degree of AR. This is similar to findings from Spain,<sup>21</sup> whereby patients in the moderate-to-severe persistent group had allergic comorbidities as high as 2.07 times those with mild-persistent symptoms ( $p = 0.0008$ ).

With regards to the compliance of intranasal corticosteroid (INS) usage among patients of different disease severities, 100% of patients in the moderate-severe persistent group used the medication consistently. This is in contrast to the INS usage of 51.7% among the mild-persistent group. Children in the mild-intermittent group had a higher rate of remission at their 3 year follow up – more than other groups with a higher severity. Rates of remission among the mild-persistent group was 52.3%, and the moderate-severe persistence group was 14.3%. This difference was statistically significant ( $p = 0.003$ ).

From this study, factors associated with HDM positivity rates were the presence of allergic conjunctivitis (96.5%), accompanied by atopic dermatitis (96.4%) and asthma (90.4%). The odd ratios for the presence of these diseases over those without were 3.06, 2.9 and 0.78, respectively. Such findings reaffirm the need for skin prick testing, especially concerning HDM rates among patients with AR and eye symptoms.

## Conclusion

House dust mites are the most important allergens causing sensitization among this group of AR children -- followed by cockroaches, cat dander and Bermuda grass. Less common allergens include careless weed, dog dander, acacia, aspergillus, cladosporium, alternaria, and Johnson and Para grasses. Besides medications, appropriate environmental control is the key success to the management of allergic rhinitis. The results from this study confirm the need to control house dust mites and cockroaches as part of an effective treatment for allergic rhinitis in children. Allergies from cats, dogs and grasses are also becoming increasingly problematic among children all over Thailand.

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