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# The Practice of Allergen Immunotherapy among Allergists in the Philippines\*

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**ABSTRACT****Background:** Allergic conditions continue to increase globally. Allergen Immunotherapy (AIT) is a therapeutic option for allergic rhinitis and asthma. This treatment can alter the natural course of the disease and provide potential cure. In the early 1970s, allergists in the Philippines began using AIT, specifically Subcutaneous Immunotherapy (SCIT). Forty years later, Sublingual Immunotherapy (SLIT) was introduced. To date, there are still no published studies on the clinical practice of AIT among allergists in the Philippines.**Objective:** The objective of the study was to assess the practice of allergen immunotherapy among allergists in the Philippines.**Methodology:** This cross-sectional study surveyed Filipino allergists in 2019. The survey consisted of a 15-point questionnaire administered to active members of the Philippine Society of Allergy, Asthma and Immunology.**Results:** Sixty allergists responded to the survey. Ninety percent of these allergists prescribed immunotherapy to their patients. Extracts used are mostly house dust mite, cockroach, grass, and animal dander. The subcutaneous route was the most frequently used (68.5%), followed by both subcutaneous and sublingual (27.8%), then sublingual alone (3.7%). Although 41 out of 60 (68.3%) allergists surveyed have not tried SLIT for their patients, these same allergists were open to the idea of using SLIT in the future.**Conclusion:** Despite difficulties in the procurement of AIT materials, Filipino allergists have been prescribing AIT for patients with allergic rhinitis and asthma as recommended by global guidelines. SCIT is more widely used than SLIT.**Keywords:** allergen immunotherapy, subcutaneous immunotherapy, sublingual immunotherapy, AIT, SCIT, SLIT

## BACKGROUND

The prevalence of allergic conditions continues to increase worldwide. Globally, 400 million suffer from rhinitis and 300 million from asthma.<sup>1</sup> In the Philippines, the prevalence of allergic rhinitis and asthma among adults is at 20% and 8.7%, respectively.<sup>2,3</sup>

Allergen immunotherapy (AIT) is a therapeutic option for allergic conditions that can alter the natural course of the disease and provide potential cure. It is a long-term disease-modifying treatment that decreases sensitivity to allergens, decreasing symptoms for many people with allergic diseases. Eligible patients for immunotherapy are those with allergic rhinitis, asthma, and atopic dermatitis who demonstrate sensitization to one or more aeroallergens.<sup>4,5</sup> Based on skin prick or serum-specific IgE test results, AIT involves repeated administration of specific allergen extracts. This treatment modality results in immunity or tolerance, providing relief of symptoms and improved quality of life even with subsequent natural allergen exposure.<sup>6</sup>

AIT was introduced in clinical practice more than a hundred years ago, but it was not until the 1900s that randomized placebo-controlled trials proved its efficacy.<sup>7</sup> The practice of AIT in the Philippines began in the early 1970s when pioneering allergy doctors founded the Philippine Society of Allergy and Immunology, later renamed the Philippine Society of Allergy, Asthma and Immunology (PSAAI).<sup>8,9</sup> For many years, subcutaneous immunotherapy (SCIT) using allergen extracts brought in from the USA by Filipino allergists was administered. Local allergens were also extracted and purified at the University of the Philippines - Philippine General Hospital. SCIT started with a build-up phase of once or twice weekly subcutaneous injections with increasing doses of allergens for 3-6 months. A maintenance phase of monthly injections ensued for 3-5 years. In 2015, the introduction of allergoid extracts from Europe allowed for a shorter build-up phase of 4 weekly injections followed by a maintenance phase of monthly shots for 3-5 years. These extracts have the advantage of decreased allergenicity while preserving the ability to elicit an immune response with less tendency for adverse reactions. In late 2018, sublingual immunotherapy (SLIT) was introduced in the Philippines.

To date, there are still no published studies on the clinical practice of AIT among allergists in the Philippines. This study surveyed Filipino allergists in 2019. The objective of the study was to assess the practice of allergen immunotherapy among allergists in the Philippines by surveying clinical practice and treatment to identify challenges and opportunities for improvement.

## METHODOLOGY

A cross-sectional design was employed in this study. An anonymous survey was conducted among active members of the PSAAI from July to August 2019. Active members who consented were invited to participate in the survey. The Quirino Memorial Medical Center ethics review committee approved the implementation of this study protocol. The study adhered to the Declaration of Helsinki.

The questionnaire administered to the respondents collected demographic information such as age, sex, and years of practice and information related to AIT, such as type and duration, indications, allergenic extracts used, and allergists' perceived patient experiences on AIT. Sublingual immunotherapy was specified as tablets in the survey as it was the only available option when the survey was distributed. The duration of immunotherapy was stratified into the following groups: 1-2 years, 2-3 years, 3-5 years, and more than 5 years.

The survey results were tabulated. Descriptive statistics such as the mean, frequencies, and percentages were used to profile the respondent Filipino allergists and their AIT-related clinical practice. Microsoft Excel was used for data processing and analysis.

## RESULTS

Sixty of 126 active PSAAI members consented and participated in the survey. The mean age of the respondents was 55.5 years, ranging from 32 to 79 years (Table 1). Ninety-three percent were females, and the majority have been in practice for more than 10 years.

Among the allergists who participated in the survey, 54 (90%) prescribed immunotherapy. The mean age of these respondents was 48.7 years, and most were females. Compared to allergists who do not practice AIT, a higher proportion of these respondents have been in practice for more than 10 years.

Most allergists who prescribed immunotherapy administer AIT of some form, including subcutaneous (68.5%), sublingual (3.7%), or both (27.8%) (Table 2). Common indications for starting immunotherapy included allergic rhinitis (98.1%), allergic asthma (98.1%), and atopic dermatitis (33.3%). The eighteen allergists who prescribed immunotherapy for atopic dermatitis also prescribed immunotherapy for allergic rhinitis and allergic asthma. However, the survey was not able to elicit from these allergists if atopic dermatitis had been the primary indication for immunotherapy. Allergens being used were sourced both locally and abroad (48.1%). Most of the

**Table 1.** Demographic characteristics of allergists who participated in the study

Characteristics	All allergists (N=60)		Allergists who practice AIT (N=54)		Allergists who do not practice AIT (N=6)	
	n	%	n	%	n	%
<b>Sex</b>						
Male	4	6.7	4	7.4	0	0.00
Female	56	93.3	50	92.6	6	100.00
<b>Age, years</b>						
30-39	14	23.3	10	18.5	4	66.67
40-49	21	35.0	20	37.0	1	16.67
50-59	19	31.7	17	31.5	1	16.67
60-69	4	6.7	5	9.3	0	0.00
≥70	2	3.3	2	3.7	0	0.00
<b>Duration of practice, years</b>						
1-5	18	30.0	14	25.9	4	66.67
6-10	8	13.3	7	13.0	1	16.67
11-20	28	46.7	27	50.0	1	16.67
>20	6	10.0	6	11.1	0	0.00

respondents in the survey have been giving their patients SCIT for a duration of 3-5 years (77.8%).

Table 3 presents the perception of allergists on their patients' experience on allergen immunotherapy. Seventy-five percent (75%) of the allergists attested that their patients strongly felt that immunotherapy was effective. Among the patients who reported immunotherapy was effective, about three-fourths (74.5%) felt relief from symptoms within six to eight months of the course of treatment.

Although 41 out of 60 (68.3%) allergists surveyed have not tried SLIT for their patients, these same allergists are open to the idea of using SLIT in the future. Among the reported adverse events of those on SLIT are oral cavity itchiness, difficulty of swallowing and breathing.

## DISCUSSION

Allergen immunotherapy (AIT) is an approach where the administration of an allergen can be used to ameliorate a specific IgE-associated response, thereby controlling allergic disease symptoms.<sup>10</sup>

AIT has been applied in clinical practice to treat patients with allergic rhinitis with or without conjunctivitis, allergic asthma, and stinging insect anaphylaxis,<sup>11</sup> of whom are willing to participate in the allergen immunotherapy treatment.<sup>12</sup> These same respiratory allergies are the indications used by the majority of the PSAAI allergists in administering immunotherapy. The use of immunotherapy in food allergies is still under investigation.

Filipino allergists followed the global standard of administering AIT to patients with allergic rhinitis and asthma, mostly with sensitivities to house dust mite, cockroach,

**Table 2.** Practice of allergen immunotherapy among allergists (N=54)

Practices related to allergen immunotherapy	n	%
<b>What kind of immunotherapy do you use?</b>		
Subcutaneous immunotherapy (SCIT)	37	68.5
Sublingual immunotherapy (SLIT)	2	3.7
Both	15	27.8
<b>For what diseases do you prescribe AIT?</b>		
Allergic Rhinitis	53	98.1
Bronchial Asthma	53	98.1
Urticaria	4	7.4
Atopic Dermatitis	18	33.3
Food Allergies	0	0.0
<b>What allergens do you use?</b>		
House dust mite	54	100
Cockroach	33	61.1
Grass pollen	22	40.7
Animal dander	14	25.9
Others, please specify	0	0.0
<b>What source of extracts do you use?</b>		
Foreign brands	23	44.2
Local (UP-PGH)	4	7.7
Both	25	48.1

UP-PGH, University of the Philippines - Philippine General Hospital

**Table 3.** Perception on patients' experience on allergen immunotherapy (N=54)

Perception on patients' experience	n	%
<b>How did your patients feel about immunotherapy?</b>		
Effective, strongly agree	39	75.0
Effective, moderately agree	13	25.0
Effective, slightly agree	0	0.0
Not effective at all	0	0.0
<b>For those who said immunotherapy was effective, on the average, how soon did your patients say they felt relief from symptoms?</b>		
6-8 months	38	74.5
9-11 months	7	13.7
12-18 months	6	11.8
19-24 months	0	0.0

grass pollen and animal dander for a period of 3-5 years. AIT for these allergens has been found to be effective.<sup>13</sup>

After a year of pharmacologic treatment and avoidance measures against HDM, immunotherapy to HDM may add clinical benefits among patients with dust mite allergy with mild to moderate asthma.<sup>14</sup> Reduction in symptoms and medication use, as well as improved quality of life, were experienced by patients with allergic rhinitis and asthma in both SCIT and SLIT with HDM.<sup>15</sup>

AIT to pollen allergens was also known to improve health-related quality of life in children and adolescents.<sup>6</sup> The inclusion of dog or cat allergens in immunotherapy should be considered when the patient has exposure to those animals. AIT to these allergens has been shown to be effective.<sup>16</sup>

Immunotherapy with cockroach extracts can also be considered. In a controlled study, patients with asthma who underwent cockroach immunotherapy for up to 5 years experienced a reduction in medication use and significant improvement in symptoms. In another study, patients with allergic rhinitis, asthma, or both who received immunotherapy with *P americana* extract for 1-year experienced significant improvement in clinical parameters. These patients also had decreased serum IgE and increased IgG4 levels after a year of immunotherapy to cockroach, demonstrating immunologic changes associated with clinical improvement.<sup>17</sup>

A meta-analysis and systematic review showed that AIT for allergic rhinoconjunctivitis is effective in improving symptoms and decreasing medication use during and after cessation of treatment.<sup>18</sup>

Allergen immunotherapy has recently been included as an effective treatment option among patients with allergic asthma.<sup>19</sup> A Cochrane review showed a decrease in bronchial hyperreactivity, asthma symptoms, and medication requirements with specific immunotherapy.<sup>20</sup> SCIT reduces long-term asthma medication use.<sup>21</sup> A large retrospective cohort study including 46,024 patients with allergic rhinitis and/or asthma showed that patients on AIT experienced minor exacerbations, fewer respiratory infections, and hospitalizations compared with controls.<sup>22</sup> Better quality of life, with reduction of symptoms, has been observed for allergic rhinitis and allergic asthma with AIT.<sup>7,18,23,24</sup>

A local study on immunotherapy among adolescents and adults showed that in the first two years of treatment, a significant decrease in the risk of new sensitization was already observed.<sup>25</sup> A similar reduction in new sensitization was observed among children.<sup>26</sup>

One year of immunotherapy significantly decreased rhinitis and asthma symptom scores and decreased the use of topical corticosteroids, antihistamines, and beta-2 agonists.<sup>27</sup> Similarly, 74.5% of allergists surveyed in our study reported that improvement of symptoms was observed by the 6<sup>th</sup> to 8<sup>th</sup> month of treatment. This finding is consistent with the REACT study wherein allergic rhinitis with or without asthma patients experienced alleviation of their symptoms and better quality of life after 1 year of immunotherapy. This was exemplified by reductions in pneumonia with antibiotic prescriptions, hospitalizations, and asthma exacerbations.<sup>22</sup>

Given potential side effects, cost, and necessary patient commitment, an important question is whether AIT provides a sustained clinical effect after treatment cessation. Clinical effects of allergen immunotherapy have different levels, but a persistent effect of up to 12 years after stopping immunotherapy has been documented.<sup>28</sup>

Filipino allergists followed the global standard of administering AIT to patients with allergic rhinitis and asthma, mostly with sensitivities to house dust mite, cockroach, grass pollen and animal dander for a period of 3-5 years.

In the Philippines, these AIT materials are not readily available for use by allergists for their patients. The difficulty in procurement and storage adds up to the cost of this treatment regimen. Hence, long-term benefits are an important consideration for its recommendation over standard pharmacotherapy. International guidelines recommend that AIT should be continued for a minimum of 3 years.<sup>29</sup>

SCIT has been the gold standard, whereas SLIT has emerged as an effective and safe alternative. Cochrane systematic reviews and meta-analyses have confirmed that both SLIT and SCIT are effective in patients with seasonal AR.<sup>30</sup> SLIT may have been introduced globally since the 1980s. Still, SLIT for house dust mite was only introduced in the Philippines in late 2018. Hence, the great majority of Filipino allergists still prescribe SCIT over SLIT, but this may very well change over time as this SLIT form of AIT may eventually become more accepted by allergists and patients as another option.

Three-year use of sublingual tablet immunotherapy has shown decreased symptoms and rescue medications, improved quality of life, and long-term immunologic changes related to tolerance.<sup>24</sup>

SCIT is relatively well-tolerated. The most common adverse effects include large local reactions defined as pruritus and erythema measuring 2.5 cm in 20-86% of

patients. In a study evaluating over 4000 injections of AIT, systemic reactions occurred in 0.24% of the injections, with all the reactions occurring when the highest allergen extract concentration was used. Local reactions may also be prevented by premedication with either antihistamines or montelukast.<sup>31</sup>

Adverse events reported for SLIT were oral pruritus, difficulty in swallowing and breathing. These local and systemic reactions have been reported with SLIT. However, it has a better safety profile and can be administered at home,<sup>11,23</sup> thus making it easier for some patients to comply.

## CONCLUSION

Although AIT has been in practice globally for more than a hundred years, it has only been in use in the Philippines for 50 years. Despite difficulties in procurement of AIT materials, Filipino allergists have been prescribing AIT for patients with allergic rhinitis and asthma for a period of 3–5 years, as recommended by global guidelines for AIT. Extracts used are mostly house dust mite, cockroach, grass and animal dander. Only recently has SLIT been introduced into the Philippine market as an alternative form of immunotherapy; hence only a few Filipino allergists have been using this form of AIT. However, since it is an oral, non-injectable form, it may become more widely used in the future with time. This survey was done pre-COVID-19 global pandemic. The practice of AIT may have altered, perhaps even with the wider acceptance and availability of SLIT. A follow-up survey to ascertain changes in healthcare systems and management is thus recommended.

## Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

## Author Disclosure

Dr. Mary Ann R. Castor is a part of the PJAAL Editorial Board. Dr. Jenifer R. Otadoy-Agustin is one of the Associate Editors of PJAAL.

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## APPENDIX

### Survey questionnaire:

This is an anonymous survey on Allergen Immunotherapy Practice in the Philippines. Answering this short survey indicates your willingness to consent to participate in said survey.

INSTRUCTION: Please encircle your answers.

1. Age / Gender
2. How many years have you been in Allergy practice?
  - a. 1-5 years
  - b. 6-10 years
  - c. 11-20 years
  - d. >20 years
3. Do you conduct immunotherapy?
  - a. Yes
  - b. NoIf your answer here is NO, WHY? You may proceed to # 13.
4. What kind of immunotherapy do you use?
  - a. Subcutaneous
  - b. Sublingual (oral)
  - c. Both
5. For what diseases do you prescribe Allergen Immunotherapy? (please encircle all applicable to your practice)
  - a. Allergic Rhinitis
  - b. Bronchial Asthma
  - c. Urticaria
  - d. Atopic Dermatitis
  - e. Food Allergies
6. What allergens do you use? (please encircle check all applicable to your practice)
  - a. Housedust mite
  - b. Cockroach
  - c. Grass pollen
  - d. Animal dander
  - e. Others, please specify
7. What source of extracts do you use?
  - a. Foreign brands, please specify
  - b. Local (UP-PGH)
8. How many years do you usually recommend for immunotherapy ?
  - a. 1-2 years
  - b. 2-3 years
  - c. 3-5 years
  - d. >5 years
8. How many have you graduated from your immunotherapy program?
  - a. 1-5
  - b. 6-10
  - c. 11-20
  - d. >20
10. How many have dropped out from your immunotherapy program?
  - a. 1-5
  - b. 6-10
  - c. >10Why? (reasons for dropping out)
11. How did your patients feel about immunotherapy?
  - a. effective , strongly agree
  - b. effective, moderately agree
  - c. effective, slightly agree
  - d. not effective at all
12. For those who said immunotherapy was effective, on the average, how soon did your patients say they felt relief from symptoms?
  - a. 6-8 months
  - b. 9-11 months
  - c. 12-18 months
  - d. 19-24 months
13. Have you prescribed oral housedust mite immunotherapy tablets?
  - a. Yes (proceed to #14)
  - b. No (proceed to #15)
14. If yes to # 13, any side effects complained, so far, by your patients?
  - a. oral cavity itchiness
  - b. difficulty of swallowing
  - c. rashes
  - d. difficulty of breathing
  - e. others (pls specify)
15. If No to # 13, do you see yourself prescribing it in the near future?
  - a. Yes
  - b. No