

Frequently asked questions in allergy practice

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Background: Over the last 10-20 years, international guidelines and consensus statements for the management of common allergic diseases (e.g. allergic rhinitis and asthma) have been developed and disseminated worldwide. However, their impact on knowledge and standard of clinical practice among primary care physicians and specialists is unknown.

Objective: To investigate need for an improvement in the dissemination of international guidelines for the diagnosis and management of allergic rhinitis.

Methods: Seven medical students who attended 3-day 1st International Basic Allergy Course (2010) took down all questions raised during the entire course. A systemic analysis of these questions was performed to identify areas for improvement in diagnosis and management of allergic diseases mainly in the Association of Southeast Asian Nations (ASEAN) region.

Results: 268 participants, 143 males and 125 females, comprising Ear, Nose and Throat (ENT) specialists (n = 106) and trainees (n = 34), general practitioners (n = 87), and other healthcare professionals (n = 41) attended the course. Of the 103 questions recorded, 59 were regarding treatment modalities in allergy practice such as immunotherapy (n = 38), pharmacologics (n = 15), nasal surgery (n = 2), and others (n = 4). 41 questions (39.8%) have answers based in the Allergic Rhinitis and its Impact on Asthma guidelines (2001 and 2008). Certain questions were selected for further analysis because they appeared to be (a) more commonly asked (e.g. immunotherapy) or (b) were deemed to be challenging or, even controversial (e.g. food allergy and differential diagnosis between vasovagal and anaphylaxis reaction), as the recommendations in current international guidelines were less well-defined.

Conclusion: Our study identified several problems that, if tackled, could help minimize confusion and provide better care for patients suffering from allergic diseases especially in the ASEAN region.

Key words: Allergic diseases; International guidelines; Management; Immunotherapy; Vasovagal and anaphylaxis reaction; Food allergy

INTRODUCTION

Allergy is one of the most common diseases medical practitioners

face, with allergic rhinitis (AR) bearing a health burden of 10 to 20% of the global population [1-3]. Being multisystemic in nature, allergy has variable clinical presentations including AR, asthma

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and eczema, with individualized impact on patients. To alleviate the symptoms of allergy which plague many in the population, there is a significant need to prioritize achieving good clinical practice in the management of patients with allergic diseases.

Using the opportunity of the 1st International Basic Allergy Course (2010), this study identifies and analyses frequently-asked questions by healthcare workers involved in allergy practice, coming from diverse backgrounds in the Association of Southeast Asian Nations (ASEAN) region. Following the 1st International Basic Allergy Course in 2010, similar questions were raised consistently throughout the subsequent courses conducted over the next 3 years. These questions are a good reflection of the common questions in allergy practice, and remain relevant today. An analysis of the collated questions points to a need for an improvement in the dissemination of international guidelines and consensus statements which have been developed to provide clinicians with basic recommendations for the diagnosis and management of AR.

MATERIALS AND METHODS

Course information

The 1st International Basic Allergy Course (2010) was a 3-day course held in Singapore which focused on basic knowledge of allergy, including pathophysiology, diagnostic approach and management. This course was jointly organized by the American Academy of Otolaryngic Allergy Society and ASEAN Rhinological Society. Other topics discussed included asthma, food allergy and the future of allergic practice. Practicum sessions on skin prick testing were also conducted for participants to gain first-hand experience. Similar courses were held in the subsequent years, namely the International Advanced Allergy Course (2011) and the Singapore Allergy & Rhinology Course in 2012 and 2013.

The 1st International Basic Allergy Course was open to all healthcare professionals. There were 268 participants, 143 males and 125 females, comprising 106 Ear, Nose and Throat (ENT) specialists, 87 general practitioners, 34 ENT trainees, 13 nurses, 10 medical students, 2 pharmacists and 16 physicians of various specialties from a total of 16 countries, where most of them were from the ASEAN countries.

Collation of questions

Question and answer sessions were held after every lecture to allow participants to raise any queries. Seven medical students

who attended the 3-day course took down all questions raised. In addition, the entire course was video recorded to ensure accuracy of transcription.

The questions were classified into various categories after careful paraphrasing, and care was taken not to alter the context of each question. The team then made reference to the 2001 and 2008 Allergic Rhinitis and Its Impact on Asthma (ARIA) documents [1, 2] for answers to the questions. Further analysis of the questions was carried out to analyze probable reasons for information gaps as well as identify areas for improvement.

RESULTS

A total of 103 questions were recorded from the course and divided into eight categories. Fig. 1 shows the distribution of the questions in each of the eight groups. The full list of categorized questions can be found in Supplement.

The most frequently asked questions were with respect to treatment in allergy practice ($n = 59, 57.3\%$) (Fig. 2). Of the 59 questions that were asked regarding treatment modalities in allergy practice, 38 were regarding immunotherapy, 15 were related to pharmacologics, 2 were related to surgery, and 4 were general questions. As most questions were on immunotherapy, we subcategorized them into methodology ($n = 15$), patient selection and indications ($n = 10$), complications of immunotherapy ($n = 8$) and evaluation of immunotherapy ($n = 5$). In the category of "patient selection and indications" ($n = 10$), 3 were regarding age criteria for starting immunotherapy, 1 regarding symptoms and severity, 5 regarding the usage of sublingual immunotherapy (SLIT) for

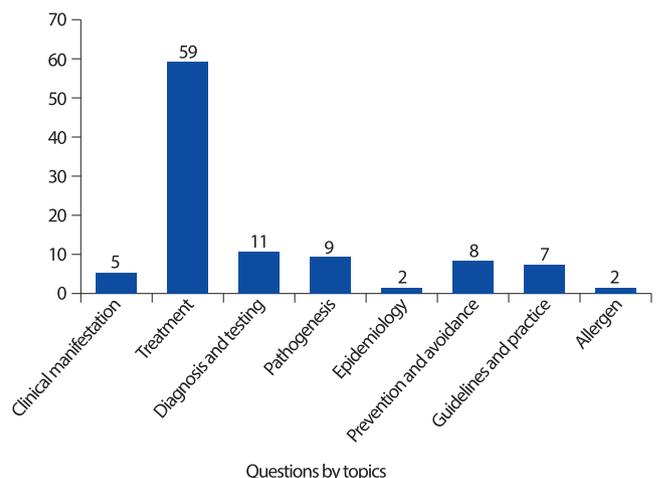


Fig. 1. Categorization of questions.

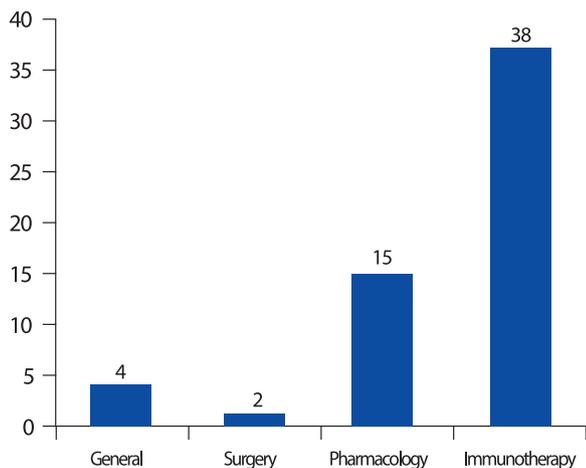


Fig. 2. Treatment questions.

different allergic conditions and 1 regarding the affordability of SLIT.

41 questions (39.8%) have answers based in the ARIA guidelines [1, 2]. Certain questions were selected for further analysis because they appeared to be a) more commonly asked or b) were deemed to be challenging, even controversial, as the recommendations in current international guidelines were less well-defined.

Questions with regards to the definition of various terms used in allergic practice were frequently raised, such as the differences between 1) “food intolerance”, “food allergy” and food hypersensitivity”, and 2) vasovagal reactions and anaphylactic/anaphylactoid reactions. As clear definition of terms would enable effective and clear communication among all healthcare workers, this paper would also be exploring these areas.

DISCUSSION

Management of allergy requires efforts from a multidisciplinary team. Although international guidelines or consensus documents have been introduced by various professional organizations in the past 10-20 years, dissemination can still be improved, especially amongst primary care physicians, who are often the first point of contact and the main providers of care to the majority of patients with allergic conditions. We have recently reported discrepancies and a lack of public education programs for AR prevention and management in Asia-Pacific countries/regions [4]. For example, there are controversies in recommended minimum age, doses and potential side-effects of many commonly used second-generation antihistamines and intranasal corticosteroids [4]. In this study,

several key recurrent themes surfaced from our analysis of the questions collated.

Frequently asked questions

Out of the 103 questions posed during the 3-day course, only 9 were related to “pathogenesis” and 2 on “epidemiology”. This does not reflect the true nature of the amount of evidence-based literature in these areas to date. This could possibly be due to the demographics of the course participants, who are mainly clinicians from the ASEAN region. There may be greater interest in topics pertaining to clinical applications and management options as opposed to academic curiosity about epidemiology and pathogenesis of allergy. More research should be carried out regionally to identify disease patterns in our geographical area and uncover any differences in disease presentation and trends as compared to Europe and the United States. This can potentially enable us to develop better management strategies to cater to patients with allergic diseases in our population.

As mentioned, 41 out of 103 questions posed during the course could be answered with information found from the ARIA guidelines [1, 2]. Many of the remaining questions can be addressed by allergy books and guidelines from other international or national bodies. This begs the question as to why lack of familiarity with the guidelines in medical practitioners persists despite easy accessibility of the ARIA guidelines. Our team puts forth certain possibilities for the situation. Firstly, we postulate that doctors may be unaware of the presence of the ARIA guidelines. Secondly, the lack of time coupled with the length of the guidelines may hinder doctors from reading them in spite of their awareness of its availability.

The ARIA guidelines are available in full version and a consolidated pocket guide form [5]. They are written for healthcare professionals like ENT specialists, general practitioners and pharmacists. As such, it can be difficult for the layperson to understand the guidelines. Therefore, more can be done to ensure the dissemination of the ARIA guidelines to members of the public apart from the healthcare fraternity. This can be achieved by publishing guidelines targeted at the laymen, with minimal medical jargon and prior medical knowledge required. We also propose that guidelines be revised to contain specific management recommendations pitched at the level of different healthcare staff in the multidisciplinary team involved in the care of the allergic patients (e.g. general practitioner, pharmacist, advanced practice nurse, ENT specialist).

Sixty-two questions (60.2%) could not be answered by information provided in the ARIA guidelines [1, 2] or the expert panel of speakers during the course. This could possibly be due to lack of evidence-based data such that the ARIA taskforce is unable to adequately provide recommendations to the masses regarding these queries. For example, it remains controversial as to when the efficacy of immunotherapy should be evaluated (from time of commencement) to distinguish between responders and non-responders to immunotherapy. More research could be done in terms of evaluating the different treatment modalities as well as developing specific step-wise algorithms for the initiation of immunotherapy. This would encourage and guide physicians who may be deterred from using such treatment due to the lack of formalized guidelines.

Food intolerance, food allergy and food hypersensitivity

Food intolerance, food allergy and food hypersensitivity are terms that have similar definitions and are often used interchangeably. Difficulties arise when diagnosing and assessing non-IgE mediated reactions to food, and this remains an area of great controversy even among highly regarded specialists in this field. General allergists in the United States [6], however, tend to use the term *food sensitivity*, which appears to be synonymous with *food hypersensitivity* used by their European counterparts [6, 7]. *Food hypersensitivity*, on the other hand, appears to be used to describe *non-IgE food allergy*. Hence, *food allergy* only encompasses IgE-mediated allergic reactions, compared to all immune-mediated allergic reactions as defined by EAACI [7].

The terminology that appears to have gained credibility [8] among healthcare providers is that adopted by the European Academy of Allergology and Clinical Immunology (EAACI) (Fig. 3) [7]. The EAACI classifies *adverse food reactions*, which are divided

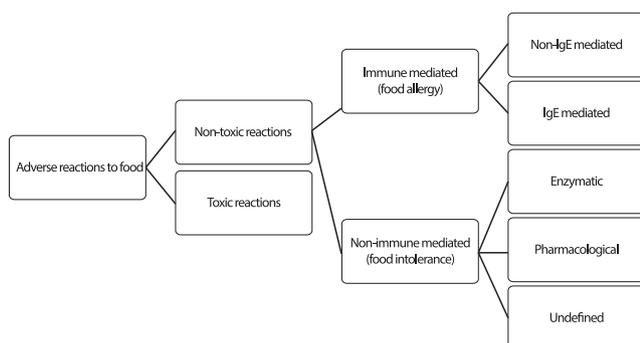


Fig. 3. Types of adverse reactions to food as classified by European Academy of Allergology and Clinical Immunology [7].

into *toxic and non-toxic reactions*. Toxic food reactions are a result of direct action of food components with no involvement of immune mechanisms. Examples of such toxic food reactions are contaminants in food. Non-toxic food reactions can be further classified into immune-mediated or non-immune-mediated reactions.

Immune-mediated *food allergy* can be subdivided into two categories, IgE mediated and non-IgE mediated food allergy [7]. While the fundamental mechanism of IgE-mediated food allergy is rather well established, the same cannot be said for non-IgE-mediated food allergies. Non-immune mediated food allergy can also be called *food intolerance*, and can be divided into *enzymatic, pharmacological* and *undefined* food intolerance. An example of enzymatic food intolerance is lactose intolerance caused by lactase deficiency. Individuals may develop food intolerance to vasoactive amines like histamines, serotonin and tyramine, known as pharmacological food intolerance. Any reproducible adverse reaction to food due to an unknown mechanism can be classified as food intolerance.

Vasovagal reaction and anaphylaxis/anaphylactoid reaction

Vasovagal reaction and anaphylaxis often present similarly, but have vastly different prognoses. Anaphylaxis is a life-threatening generalized or multisystemic hypersensitivity reaction [8], triggered by exposure to antigens. Immediate treatment is imperative as mortality rate approaches 10% in anaphylactic shock [9]. Vasovagal reactions, following painful interventions such as injection, are commonly confused with anaphylactic reactions. Given the severity of the latter, it is of paramount importance that health professionals are able to differentiate between the two reactions without delay.

Signs and symptoms observed in vasovagal or anaphylactic reactions can be classified according to systems: cardiovascular, respiratory, skin, central nervous system and genitourinary (Table 1) [6, 10]. In anaphylactic reactions, the organs richest in mast cells are primarily affected – respiratory tract, blood vessels and skin. Unsurprisingly, the differences between the two reactions in these three systems are also most pronounced.

In anaphylactic reactions, the patient would be hypotensive and tachycardic, with a weak or absent central pulse. He/she would have generally flushed, warm skin; little perspiration, and may be cyanotic late in the episode. Contrastingly, if the patient were experiencing a vasovagal episode, he/she would have

Table 1. Summary of the main differences in clinical signs and symptoms between vasovagal and anaphylaxis [6, 10]

Observations	Vasovagal	Anaphylaxis/ anaphylactoid
Cardiovascular system		
Pulse	Bradycardic	Tachycardic
Blood pressure	Normal	Hypotensive
Respiratory system		
Hoarseness	Absent	Progressive
Cough, wheeze, stridor	Absent	Present
Skin		
Color	Pale	Red (cyanosis presents late)
Angioedema, urticaria	Absent	Present
Onset		
Time	Almost immediate	Within minutes – hours

a slow pulse rate with a strong central pulse. Blood pressure could be low to normal; hypotension should be only transient and would be corrected in the supine position. Pale and cool skin with generalized pallor and profuse perspiration may be observed. Angioedema, urticaria, conjunctivitis and rhinitis seen in anaphylactic patients would be absent in patients with vasovagal reactions.

Patients experiencing an anaphylactic reaction may present with itchy mucous membranes of the respiratory tract, increased nasal secretions or congestion, and progressive hoarseness of voice. They may be coughing, wheezing and dyspnoeic. Patients could also experience nausea, diarrhea, abdominal pain, urinary urgency and uterine cramps late in the anaphylactic episode. On the other hand, patients with vasovagal reactions would not experience any changes in their respiratory tracts, genitourinary or gastrointestinal systems. The loss of consciousness in patients with a vasovagal episode would be transient, and they may be anxious during the consultation. On the contrary, patients with anaphylactic episodes would lose consciousness only later, and they would have a feeling of impending doom. It is also important to note that the onset of vasovagal reactions is almost immediate, within minutes of inoculation, while it may occur in minutes to hours in the case of anaphylactic reactions.

In conclusion, our study identified several problems that if tackled, could help minimize confusion and provide better care for patients suffering from allergic diseases. Also, to leverage on the multidisciplinary approach to allergy, it is important to pitch recommendation guidelines at the level that different healthcare

workers involved in allergy management are able to provide. Deeper research into the emerging areas in allergy management such as immunotherapy should be done so that physicians are provided with clearer guidelines and algorithms to start treatment in their patients confidently, and troubleshoot potential problems in the process.

SUPPLEMENTARY MATERIALS

Supplementary material can be found via <http://apallergy.org/src/sm/apallergy-4-48-s001.pdf>. Supplementary material: Questions asked in the 1st International Basic Allergy Course.

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Supplement – Questions asked in the 1st International Basic Allergy Course

1. CLINICAL MANIFESTATION

What is the percentage of people who have both combined food and inhalant allergy?

What is the difference between seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR)?

What is the reason for the difference in peak timing for PAR and seasonal allergic rhinitis SAR?

Some patients report sneezing or exacerbation of allergic rhinitis (AR) symptoms when washing face with cold water or touching their noses. Is there an explanation for this?

Till what age will AR persist?

TOTAL: 5

2. TREATMENT

I. General

Are there different treatment methods for different types of allergic disease? How can we ascertain what methods to use?

For patients with combined allergies, will treating the inhalant allergies alleviate the food allergies as well?

In Singapore, topical antihistamines are not available. What can be used to replace them?

If an allergic patient suffers from chronic inflammation of the nose due to anatomical variation in the osteomeatal complex (OMC), how long should medical treatment be administered before surgical intervention?

TOTAL: 4

II. Surgery

How would you manage septal deviation caused by turbinate hypertrophy?

For which type of AR patients would the use of surgery be considered?

TOTAL: 2

III. Pharmacology

How would you manage septal deviation caused by turbinate hypertrophy?

For which type of AR patients would the use of surgery be considered?

What is your view on the use of decongestants in children?

Is it safe to use intranasal corticosteroids in young children less than 1 year of age?

Anti-Leukotriene Receptor Agonists (Anti-LTRA) are recommended for adults and children greater than 6 years of age. What are the recommendations for children below 6 years?

Are they indicated only for SAR?

What is the dosage and treatment duration recommended for the use of oral and intranasal steroids in adults respectively?

Do you recommend the use of montelukast as first line therapy for asthma?

Could a patient be placed on both inhaled and intranasal corticosteroids?

It is recommended that antihistamines/intranasal corticosteroids are used in the morning. Does using it at other times of the day affect its effectiveness?

Is there a difference in effectiveness of intranasal steroids when taken at one sitting (2 puffs qd) and splitting it up into 2 doses (1 puff bd)?

Is there a difference between giving intranasal steroids upright and in the 'Mecca' position?

Should intranasal steroid be prescribed for a patient having bad rhinorrhea?

In your practice, what is the youngest age of the patient you have given intranasal steroid to?

How long should the treatment period be?

What is the recommended dose?

Is there a preferred intranasal steroid to prescribe for children?

Why are antileukotrienes only indicated in SAR? Is it due to their decongestant effect?

ARIA guidelines recommended the prescription of oral steroids in SAR. What is the dosage and for how long should it be used?

In the study 'Clinical and immunologic effects of Sublingual Immunotherapy (SLIT) in patients with PAR: a double-blind, placebo controlled study', Staloral is used 10 drops daily; whereas the recommended dose is 4 drops daily. Why is a higher dose used in the study?

women

TOTAL: 15

IV. Immunotherapy

Is there a minimum age and maximum age for administration of immunotherapy?

Can sensitivities to multiple allergens be treated together, or should they be treated separately?

Before starting the patient on SLIT, should a quantitative test be performed?

Where can the phenylated saline and glycerin be obtained for preparation of the vial of allergen mixture used during immunotherapy?

Can normal saline be used instead of phenylated saline?

Is it advised to treat patients with mild allergies to certain antigens?

Should allergy testing be repeated on a patient referred from another doctor? Could the patient's existing results be used?

If a patient has a wheal of diameter 13mm response to the most diluted vial, is it safe to start therapy with that vial?

Since the volume of antigen is so small, what kind of syringes should be used?

What precautions could be used to prevent the antigen from sticking on the walls of the micropipette tips?

What are your thoughts on Rush Immunotherapy?

Which is a preferred treatment method?

What happens if the antigen used for testing and the antigen being administered in the vial comes from a different supplier? Can we use different antigen source in testing and administration?

Do you do the mixing of the vials yourself?

At the point of concentrate, can more than 5 antigens be mixed?

What is the criteria for which immunotherapy is indicated?

During treatment, would a rise in blocking IgG imply that immunotherapy is not working?

In an event where treatment is halted, when should the vial test be performed again?

Should it be done during the escalation phase?

Should it be done during the maintenance phase?

Although it is convenient, is vial-mixing safe and evidence-based?
Should mixing of each antigen be done individually?

Is EpiPen given intramuscular or intravenously?

How should patients be monitored during immunotherapy treatment other than observing the change in frequency and severity of symptoms?

What are the criteria for prescribing antihistamines for allergic reactions after immunotherapy?

Will there be changes in blood parameters after a few years of immunotherapy?
Can this be used to test the effectiveness of immunotherapy?

If a patient has an anaphylactic reaction during the build up phase of immunotherapy, should treatment be continued?

Have there been anaphylactic reactions to immunotherapy?

When a patient on beta-blockers has an anaphylactic reaction, epinephrine will be administered and anti-hypertensives prepared in case of high blood pressure. Is the procedure the same for non-hypertensive patients?

In Subcutaneous Immunotherapy (SCIT), groups of allergens are put into different vials to avoid proteolytic action of a group of allergens on another. Does the same concept apply to SLIT?

Does the same protocol for immunotherapy apply to paediatric patients?

When should the efficacy of the immunotherapy treatment be evaluated?

What kind of medications should be avoided during SLIT?

Is SLIT effective for treating food allergy?

Should patients undergoing immunotherapy be placed on antihistamines and topical ICS (or should they go cold turkey)?

With the new 5-day up-dosing method for SLIT (as opposed to 12 weeks), will we expect more side effects to occur? Should patients undergoing this be placed on antihistamines/steroids?

In my country, the use of SLIT is very expensive (about 4 times that of SC). Is that also the case in US?

In your study, there is no decrease in IgE levels after a year. When do you expect the immunotherapy to start having an effect on IgE levels?
Did you follow-up on your patient's symptoms after the study ended?

Does immunotherapy have a role in treating asthma?

When is the best time to start immunotherapy?

What is the minimum age for children to start immunotherapy?

When should a vial test be done after therapy has been discontinued for some time? What if there are discrepancies in earlier slots?

If 10 allergens were placed in the maintenance vial, should 50% glycerin be added?

Do you use the same concentrate for SLIT as that for SCIT or do you use a special extract for SLIT? What is the difference between the extract used for SCIT and the one sold in EU for SLIT?

TOTAL: 38

GRAND TOTAL: 59

3. DIAGNOSIS AND TESTING

What kind of testing can be done for idiopathic rhinitis?

With the focus on IgE testing, will non-IgE causes of idiopathic rhinitis be missed?

What kinds of tests are used to diagnose allergy?

How should Skin Prick Test (SPT) results be evaluated?

Should all patients with rhinitis be subjected to SPT?

How should patients with dermatographism be handled?

Between SPT and Modified Quantitative Testing (MQT), which is better based on the evidence?

Based on current evidence, is SPT or Multi-Prick Test (MPT) a better diagnostic tool?

In selecting an antigen for SPT, is it possible to use fresh specimen antigen? (For example: Flour for patient who works in a bakery) If possible, how should the antigen be prepared (in terms of weight/volume)?

Is SPT more likely to generate a false positive or false negative?

What is the easiest (i.e. most user-friendly/convenient) test to identify skin allergies?

TOTAL: 11

4. PATHOGENESIS

What is the mechanism in allergic rhinitis that causes more severe attacks in the morning?

What is the immunological difference between SAR and PAR?

Does asthma cause tissue remodeling?

Is there an immunological reason causing children to be more affected by allergies than adults?

Why are allergies prevalent in childhood?

Is it good that the prevalence of allergies decreases?

After surgical treatment of sinusitis, allergic patients tend to fare worse than non-allergic patients. How do we diagnose and assess allergy? Which tests would you recommend?

Other than being weaker immunologically, why else is the occurrence of AR lower in elderly patients?

Why does regular frequent exposure to allergens not imitate immunotherapy, which produces blocking IgG?
E.g.: working in dusty environment and being allergic to house dust mites (HDM).

TOTAL: 9

5. EPIDEMIOLOGY

What protocols are there in place to maintain the facts and figures for the prevalence of allergies in the US, especially since US is vast with different living conditions and vegetations?

Why is there a rise in peanut allergies within the last 10 years?

TOTAL: 2

6. PREVENTION AND AVOIDANCE

Apart from washing linen at 60 degree Celsius, what else can patients do to get rid of the dust mites?

What is the percentage of tannic acid in regular black tea? Could regular tea be used in place of the costly tannic acid solutions available in the market?

In my hometown, patients are recommended to change the High Efficiency Particulate Air (HEPA) filter after every 2 years, if they can afford it. However in your presentation, it is advised that the filter be changed every 3 to 6 months. Would this not incur a high cost? Is this the recommendation in the US?

Can regular air filters/other filtration devices be used in place of HEPA filters?

According to Evidence-Based Medical Practice (EBMP), are avoidance measures helpful?

Which avoidance measures are mentioned in studies?

Which avoidance measures can be used in combination?

What is the strength of recommendation in using avoidance and environmental control for patients based on the evidence available?

To what extent do environmental chemicals and toxins contribute to allergies? Would becoming more environmentally friendly help?

What is the recommended bleach dilution for washing of linen?

How can we be sure that agents/allergens do not cross react?

TOTAL: 8

7. GUIDELINES AND PRACTICE

How can anaphylactic reaction and anaphylaxis be differentiated clinically?

Is it standard practice for staff (including nurses) to be BCLS/ACLS-certified?

Is there a need for the clinic to be situated near the emergency department or coronary care unit?

Are the terms "food intolerance", "food allergy" and "food hypersensitivity" used interchangeably?

Do respiratory physicians in the US recommend immunotherapy?

Would you recommend the use of peak flow metres for self-monitoring at home?

Given that the efficacy of immunotherapy is in the range of 55 – 80%, in patients who do not experience improvement of symptoms or decreased medication use, when do you decide to stop therapy? What time frame would you give for immunotherapy to take maximal effect before stopping in 'non-responsive' patients?

TOTAL: 7

8. ALLERGEN

Is the peanut allergen presented differently when prepared in different ways?

What is your opinion on the possible impact of genetically-modified rice with peanut genes?

TOTAL: 2