CME Article

Allergic rhinitis: evidence-based practice

Lim M Y, Leong J L

ABSTRACT

Allergic rhinitis is a common condition in Singapore, with a considerable disease burden. This article reviews the latest evidence-based concepts and current understanding of the disease, including its aetiology, pathogenesis, signs and symptoms, investigations as well as management. Particular attention is given to reviewing principles that will aid the management of this disease from a practical point of view, and the latest evidence for the various pharmacological options as well as immunotherapy is discussed. The article should be of interest to otolaryngologists as well as allergists, respiratory physicians and family practitioners.

Keywords: allergic rhinitis, diagnosis, nasal inflammation, review, treatment

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INTRODUCTION

Rhinitis is simply inflammation of the lining of the nose. There are different causes for rhinitis, including infectious, autoimmune and vasomotor causes, but allergy is the commonest cause. Allergic rhinitis (AR) can be a considerable source of morbidity in poorly managed patients. It impairs social and work functions, and can significantly affect the patient's quality of life. The condition is relatively common worldwide, especially among the young. Local population-based studies have reported a prevalence of AR in 44% of Singaporean school children.[1]

DEMOGRAPHICS

AR can occur at any age, but most patients develop the condition before the age of 30. Both males and females are equally affected, although there is a preponderance of male paediatric patients.[2]

AETIOLOGY

The common offending allergens in Singapore include house dust mites, pet allergens and cockroaches. In countries with seasonal variations, pollen, including tree, grass and weed pollen, is a common cause of AR. A retrospective study of 1,000 patients undergoing skin prick testing (SPT) performed at the Ear, Nose and Throat Centre of the Singapore General Hospital between January 2004 and January 2005 revealed that the local population is more sensitised to indoor rather than outdoor allergens (Table I) (unpublished data).

Table I. Results of skin prick test done on the local population (unpublished data).

Allergen	Sensitisation profile(%)
House dust mites*	
Dermatophagoides farinae	83.9%
Dermatophagoides pteronyssinus	81.7%
Cockroaches	
America	60.7%
Germanic	55.1%
Outdoor allergens	
Bahia grass	23.1%
Mugworth common	17.4%
Bermuda grass	17.3%

*Data for *Blomia tropicalis* is not available in the above study, but based on another local study, its sensitisation profile approximates 70%.[3]

PATHOPHYSIOLOGY

Inhaled allergens interact with T-cell and B-cell lymphocytes, and with the help of cytokines, result in the production of IgE antibodies. These antibodies attach to the mast cells and circulating basophils. A second exposure to the same allergen leads to degranulation of the mast cells and basophils. This results in the release of several mast cell mediators, including histamine, prostaglandin D2, leukotrienes and tryptase.

An early phase reaction occurs in response to the release of these mediators. Stimulation of the mucous glands and increased vascular permeability with plasma exudation cause an increase in nasal secretions. Vasodilation results in a sensation of congestion, while histamine-induced stimulation of the sensory nerves located in epithelial tight junctions leads to sneezing and itching. A late phase, which occurs in a proportion of patients, starts at four hours and peaks at six hours,

Department of Otolaryngology, Singapore General Hospital, Outram Road, Singapore 169608

Lim MY, MRCS, DOHNS, MMed Registrar

ASCENT Ear Nose and Throat Specialist Group, 3 Mount Elizabeth, #08-01, Mount Elizabeth Medical Centre, Singapore 228510

Leong JL, FRCS Director and Consultant

Correspondence to:
Dr Leong Jern-Lin
Tel: (65) 6738 3615
Fax: (65) 6738 3937
Email: entdrleong@gmail.com

and lasts up to days. The late phase is characterised by the deployment, activation and perpetuation of inflammatory cells at the nasal mucosa, including neutrophils, basophils, eosinophils, lymphocytes and macrophages. This results in continued inflammation. Cytokines and chemokines are central to the regulation of this late phase. The symptoms of the late-phase response are similar to those of the early phase, with less sneezing and itching but more congestion and mucus production.

An important phenomenon that is observed in AR is the priming effect, where nasal provocation with an allergen in a nasal mucosa that has recently been exposed to the same or another allergen (and therefore already inflamed and "primed") requires a much smaller allergen burden in order to induce allergic symptoms. The mechanism of this phenomenon seems to be related to the mucosal influx of eosinophils or priming of inflammatory cells by cytokines.[4-6] Systemic effects such as tiredness and malaise can arise from the inflammatory response, thereby impairing the patient's quality of life.

SYMPTOMS AND RELEVANT HISTORY

The symptoms of AR include nasal obstruction, rhinorrhoea, anosmia, loss of taste, sneezing, itching of the nose and headache. A history of related conditions, such as conjunctivitis, asthma and atopic dermatitis, should be noted. Complications of AR, such as sinusitis, otitis media, sleep disturbance, apnoea or dental problems, may also be present. Other relevant questions to be asked as part of history-taking are the time course of the disease, age of onset, family history, possible triggers of symptoms (including occupational and home exposures), response to medications, and effects on work and quality of life.

EXAMINATION FINDINGS

The nasal examination of AR patients shows a bluish-grey discolouration and oedema or erythema. Clear watery rhinorrhoea may be seen. Signs of "allergic salute" (horizontal crease across the nasal supratip, produced by repeated upward stroking of the nasal base) and "allergic shiner" (dark circles around the eyes that are related to nasal vascular congestion) may be present. Examination of the ears may reveal evidence of eustachian tube dysfunction or otitis media, which are both complications of AR. The posterior oropharyngeal wall may demonstrate "cobblestoning".

INVESTIGATIONS

Blood tests

Blood eosinophil count and total serum IgE level tend to be elevated in AR, although clinically, these tests on their own are not very useful, as the diagnostic sensitivity and specificity for both are suboptimal.

Nasal cytology

Scrapings of secretions and nasal mucosa cells can be taken; in AR, an increase in the number of eosinophils is observed, although this also occurs with nonallergic rhinitis with eosinophilia.

Allergy testing

The purpose of allergy testing is to determine which antigens a patient is allergic to, thereby enabling the development of strategies to avoid these allergens. Several methods are available:

(1) Scratch testing: The skin is scratched to remove the overlying keratin, and an extract of the test allergen is then placed over this area. This method lacks sensitivity and should not be used.

(2) SPT: One drop of the antigen is placed on the skin and introduced by puncturing the skin with a lancet. Histamine is released during the early phase reaction as a result of the antigen binding to IgE on the skin mast cells. This is the commonest method of allergy testing used in the clinical setting as it is a fast and reasonably reliable method. There is a low risk of anaphylaxis with this test. SPTs should be interpreted in the light of the clinical history. At least 15% of people with a positive PT do not develop symptoms on exposure to the relevant allergen.[7] SPTs have a high negative predictive value. Clinically, it is important to note that SPTs are suppressed by antihistamines and topical skin, but not by oral steroids.[8] Testing kits are increasingly being improved upon, and the Multi-Test® II allows multiple skin tests to be performed at an unparalleled speed of 24 tests in 30 seconds.

(3) Intradermal dilution testing (IDT): This method involves the intradermal injection of varying concentrations of the antigen and allows for the determination of the dilution endpoint. This is the weakest dilution that produces a positive skin reaction and is hence the strongest starting dose of immunotherapy that may be safely administered. Employing IDT to guide immunotherapy shortens the time required for a patient to reach his individual maximally tolerated dose and ultimately translates into health cost savings.[9]

(4) *In vitro* allergy tests: Radioallergosorbent test is the

commonest of these tests, in which serum is obtained to quantify the amount of specific IgE to individual allergens. The advantage of this test is that it avoids the risk of anaphylaxis, is suitable for young children as it is less traumatic, and may be more appropriate in patients with severe skin eczema, where SPTs may be difficult to read.

DIAGNOSTIC DILEMMAS: DIFFERENTIATING AR FROM OTHER SIMILAR CONDITIONS

It is imperative to distinguish AR from other conditions with overlapping spectrum of symptoms, since the aetiology and management of these conditions differ.

Difference between AR and non-allergic rhinitis

First and foremost, AR is much more common than the other forms of rhinitis. Symptomatically, although congestion is common in both allergic and non-allergic rhinitis, anterior rhinorrhoea tends to be more common in AR while postnasal drip tends to be more common in non-allergic rhinitis.[10] Pruritis and sneezing is less common in non-allergic rhinitis than in the allergic form.

Examination in AR reveals pale, bluish-grey, boggy, swollen mucosa, while non-allergic rhinitis is more likely to simply present with erythematous mucosa, although this may also be the only finding in AR. There may be exacerbating factors (e.g. exposure to dust) or seasonal variations in AR. Family history and other allergic diseases may be present in AR, and skin prick tests are more likely to be positive. The improvement of symptoms with antihistamines and corticosteroids points to AR, although non-allergic rhinitis may also respond to these medications.

Difference between AR and chronic sinusitis

It is useful to distinguish clinically between AR and chronic sinusitis since these are two separate entities. The current consensus is that although there is increased prevalence of AR in patients with chronic sinusitis, the exact role of allergy in sinusitis remains unclear.[11] Both clinical entities may present with blocked nose, rhinorrhoea and anosmia. However, the rhinorrhoea tends to be clear and watery in AR, whereas in sinusitis, it tends to be thicker and more purulent. Sneezing and nasal itch with or without conjunctivits are more common in AR, whereas facial pain is more common in chronic sinusitis.

The inferior turbinates take on a bluish hue in AR. In contrast, patients with chronic sinusitis may have polyps, oedema/mucosal swelling or mucopurulent discharge from the middle meatus. SPTs are more likely to be positive in AR. However, AR and chronic rhinosinusitis can co-exist in the same patient, and SPTs should be performed in all suspected cases of chronic rhinosinusitis in order to optimise treatment.

EDUCATION AND ENVIRONMENTAL CONTROL

Education of the patient is an important part of disease management. Patients should be educated regarding the causes, symptoms and therapy (including environmental control) required for their condition. Education is likely to encourage better compliance with allergen avoidance and pharmacotherapy.

Allergen avoidance may be helpful in some instances. For dust mite allergy, dehumidification is useful, as mites require 50% or more humidity. Rigorous attention should be paid to a household minimal dust policy. This includes the removal of carpeting, efficient vacuuming (preferably not by the patient, and if so, while wearing a face mask), covering of the mattress and pillows with impermeable covers, washing of bed sheets regularly in hot (at least 55°C) water to kill any mites present. Due to the ubiquitous nature of dust and house dust mites (HDM), mutiple avoidance measures are required to obtain maximum benefit from HDM allergen avoidance.[12-13]

For animal allergy, removal of the offending pet is the best solution. Some patients cannot do without their pet and if so, it is best to keep the pet out of the bedroom in a non-carpeted room. Six months or more are required for animal dander to clear; hence, trials of brief pet removal are often ineffective.[14] Other measures include employing high-efficiency particulate air filters and improving ventilation in rooms where the patient spends most of his time. Though inconvenient, bathing the cat weekly may be useful. Measures to exterminate cockroaches may be helpful for cases of cockroach sensitivity.

PHARMACOTHERAPY

There are many different forms of pharmacotherapy available in the market.

Oral antihistamines

These include first-generation antihistamines such as chlorpheniramine (Piriton®) and diphenhydramine (Benadryl®), second-generation antihistamines such as cetirizine (Zirtec®) and loratidine (Clarityn®), and third-generation antihistamines such as levocetirizine (Xyzal®),

desloratidine (Aerius®) and fexofenadine (Telfast®).

The mechanism of action involves histamine H1 receptor sites, thus blocking the effects of histamine. However, there are also anti-allergic properties besides H1 blockage.[15] The onset of action ranges from one to three hours,[16] with variable lengths of efficacy (up to 24 hours) depending on the antihistamine used.

Antihistamines are more effective in the amelioration of rhinorrhoea, itch and sneezing rather than nasal obstruction. They have been shown to reduce the total nasal symptom scores by a mean of 7% more than a placebo and to improve the patient's quality of life.[17,18] Importantly, it has also been shown that the regular use of antihistamines rather than 'as required' therapy is more effective.[19] The sedative effect of first-generation antihistamines is minimal in comparison to that of the second- and third-generation antihistamines.

Topical antihistamines

Intranasal antihistamines such as azelastine have been shown to have a fast onset of action (15 minutes) and are also more effective than oral antihistamines for rhinitis symptoms.[20,21] In addition, they are more rapidly effective than topical steroids, but in the long term, their effects are less potent[22] and less cost effective compared to those of topical steroids.[23] Currently, intranasal antihistamines are not actively marketed in Singapore, although azelastine is registered for use. No significant sedative effect is produced with topical administration.[24]

Decongestants

Decongestants work by activating alpha-adrenergic receptors in the nasal mucosa, thereby causing vasoconstriction. These include α1-adrenergic agonists (phenylephrine), α2-adrenergic agonists (oxymetazoline) and noradrenaline releasers (ephedrine and pseudoephedrine). The onset of action for intranasal decongestants is within ten minutes. Both phenylephrine and oxymetazoline last for more than six hours. The prolonged use of intranasal decongestants (> five days) leads to rebound rhinitis medicamentosa, and should thus be avoided. Oral decongestants have a weaker action on obstruction than intranasal decongestants, but they do not cause any rebound effect.

Intranasal glucocorticoids

Glucocorticoids are the most effective pharmcotherapeutical option available in the treatment of AR. Glucocorticoids work by binding to a glucocorticoid receptor in the cytoplasm, forming a complex that moves into the nucleus to affect gene transcription. The result is a down-regulatory effect on inflammatory cells and cytokines involved in the pathogenesis of AR. In addition, glucocorticoids have been shown to reduce the release of histamine[25] and leukotrienes,[26] as well as to inhibit seasonal increases in ragweed IgE antibodies.[27] The commonly used intranasal glucocorticoids include mometasone furoate (Nasonex®), triamcinolone acetonide (Nasocort®), fluticasone propionate (Flixonase®), beclomethasone dipropionate (Beconase®) and budesonide (Rhinocort®)

Glucocorticoids have a slower onset of action than antihistamines, occurring within six to eight hours after the first administration. Their effects may not be immediately apparent (takes up to a few days), and the maximum efficacy may not be apparent until after two weeks.[28] However, they have been shown to be superior to antihistamines,[29] and to reduce all symptoms of rhinitis by 17% more than a placebo.[17] Regular usage, with a titration at the lowest effective dose, is required in order to benefit fully from glucocorticoids.

The local side effects include crusting, dryness and minor epistaxis, but these are usually mild and transient. Except for dexamethasone and betamethasone drops that have a higher systemic absorption, intranasal glucocorticoids have no effect on the hypothalamic-pituitary-adrenal axis. Long-term growth studies in children using fluticasone, mometasone and budesonide have shown reassuring safety data, unlike beclomethasone.[30] Currently, mometasone is licensed for use in children above the age of two years and flixonase, for children above the age of six years.

Topical anticholinergics

Topical anticholinergics such as ipratropium bromide work by blocking the muscarinic receptors of nasal glands supplied by parasympathetic fibres from the sphenopalantine ganglion. Its onset of action is 15–20 minutes, and it is effective in controlling rhinorrhoea but not other nasal symptoms.[31-33]

Regular use of topical anticholinergics is required in severe rhinorrhoea for patients with perennial rhinitis.[34] Their use in combination with a nasal steroid should be considered in patients whose rhinorrhoea is one of the predominant symptoms, as combination use is more effective than either treatment modality on its own.[35] Occasional use is helpful in patients with infrequent attacks of nasal hypersecretion, and as the onset of action is immediate, it can also be used before exposure to known provocating factors.[34] The side effects include dry nose and epistaxis, with rare systemic

anticholinergic effects.[30] Nasal spray ipratropium bromide is currently not registered for use in Singapore but is available in certain hospitals by special request.

Leukotriene receptor antagonist (LTRA)

LTRA acts to inhibit the cysteinyl leukotriene receptor and prevents the action of leukotrienes released by mast cells. The most well known of these antagonists is montelukast. LTRAs have been shown to have a similar therapeutic profile to antihistamines and are hence a viable alternative to them. A recent qualitative meta-analysis has shown that LTRAs improved the composite nasal score by 5% more than a placebo and improved the quality of life in seasonal AR. By comparison, antihistamines were observed to improve the composite nasal symptom score by 2% more and intranasal corticosteroids, by 12% more than LTRAs. The combination of an LTRA and antihistamine was also shown to be significantly more effective than either agent used alone; however, the differences were not significant in terms of quality of life.[17] Combination therapy is not recommended by the British Society for Allergy and Clinical Immunology.[30] LTRAs are usually well tolerated, with the occasional headache, gastrointestinal symptoms or rashes reported.[30] Montelukast is also beneficial to patients with asthma and is therefore especially useful in patients with both AR and asthma.

Intranasal cromolyns

Intranasal cromolyn stabilises and inhibits the degranulation of mast cells. Like corticosteroids, it has preventive action and is hence effective in both the prophylaxis and treatment of seasonal AR.[36,37] However, it is not as efficacious as intranasal antihistamines or intranasal glucorticoids,[38,39] and if used, it should only be employed in patients with mild symptoms.[40] The onset of action is a few days and the peak effect may not be noticeable for up to two weeks.

Due to its relatively weak effect, intranasal chromolyn is not a major therapeutic option for adults in the treatment of AR, although it can be used in the treatment of allergic conjunctivitis. It is a safe drug and hence a viable choice in pregnant women and children. The symptoms of sneezing, rhinorrhoea and itching are usually better controlled than nasal obstruction.[41] The side effects include nasal irritation, headache, occasional taste disturbance and rarely, bronchospasm.[30] Nasal spray sodium cromoglycate is currently not registered for use in Singapore.

CHOICE OF THERAPY

The eventual choice of pharmacotherapy depends on the severity and type of symptoms, as well as whether symptoms are intermittent or persistent. The updated Allergic Rhinitis and its Impact on Asthma document has produced guidelines in line with the following considerations:[24] (1) Mild intermittent disease: Options are oral or intranasal H1-antihistamine and/or decongestant or leukotriene receptor antagonist; (2) Mild persistent disease or moderate/severe intermittent disease: Options (not in preferred order) are oral or intranasal H1-antihistamines and/or decongestant or intranasal corticosteroids or leukotriene receptor antagonist (or cromone). In the case of mild persistent disease the patient is to be reviewed after 2–4 weeks, and medications should be stepped up if there is no improvement; (3) Moderate/severe persistent disease: Options in preferred order are intranasal glucocorticosteroids, H1-antihistamine or leukotriene receptor antagonist. The patient should be reviewed in 2–4 weeks. If there is improvement, the medication should be continued for at least one month with gradual step down. If there is no improvement, the diagnosis or compliance has to be questioned, and the possibility of infection has to be considered. The dose of intranasal corticosteroid can be increased. Ipratropium can be added for rhinorrhoea, and decongestants or short term oral corticosteroid can be prescribed for blockage symptoms. Patients who fail this regime should be referred to a specialist.

IMMUNOTHERAPY

What is immunotherapy?

Immunotherapy (IT) is the practice of modulating the immune system by the administration of gradually increasing doses of an allergen to an allergic subject. The ultimate goal is to reduce the symptoms and requirement for rescue medication associated with subsequent exposure to the allergen in question.

Mechanism and effects of IT

The mechanisms behind IT are complex and unclear, but the basic principles are: (1) Modification of allergen-specific T-lymphocyte responses, which affect downstream antibody synthesis and activation of inflammatory cells;[42] (2) Transient increases in allergen-specific IgE followed by blunting of seasonal increases of IgE;[42,43] (3) Increase in allergen-specific IgG antibodies, and in the case of subcutaneous immunotherapy (SCIT), increase in IgG4 subclass in particular.[42] IgG4 are "blocking" antibodies that inhibit IgE-mediated anaphylaxis through both IgE-allergen interception and Fc gamma RIIb cross-linking;[44] (4) Reduction in inflammatory cell recruitment and activation.[24,42]

By these mechanisms, IT reduces the severity of the allergic disease to a certain antigen and the need for anti-allergic drugs, and improves the quality of life.[45] It also alters the natural course of allergy by preventing the development of new sensitisations,[46] as well as stops the development of asthma in patients with only allergic rhinoconjunctivitis.[47]

Methods of delivery

Allergen vaccines can be delivered orally, nasally, subcutaneously or sublingually. SCIT and sublingual immunotherapy (SLIT) are the most widely used methods for vaccine administration. Allergen vaccines can be unmodified preparations or chemically modified (e.g. formaldehyde allergoids), which can make IT more effective or reduce the risk of side effects.

Indications, evidence for use and efficacy

Indications for IT include patients with rhinoconjunctivitis and/or asthma caused by pollen (grass or tree) or HDM allergy. Evidence is emerging for the use of IT in the treatment of rhinitis due to other allergens. Patients should have either demonstrated a poor response or side effects to pharmacotherapy, or are unwilling to receive long-term pharmacological treatment.

The existing levels of evidence in IT are Level 1a evidence (meta-analysis) for the use of SLIT in the treatment of rhinitis and asthma and SCIT in the treatment of asthma, as well as Level 1b evidence for the use of SCIT in the treatment of rhinitis.[42] The efficacy of SCIT is close to 50%–60% in some studies.[48,49] A local study conducted in Singapore showed that rhinitis symptom control after two years of SCIT was excellent in 32.5%, good in 45.6% and fair in 14.2% of patients. No improvement was observed in 7.7% of the patients. There were only five limited systemic reactions, constituting 0.008% of injections, during the two-and-a-half year mean immunotherapy treatment course.[50] In employing SLIT, a 16%–30% reduction in the symptom scores and a 28%–38% reduction in the medication scores were observed compared with the placebo.[51,52] The efficacy of SLIT as compared with SCIT is still not clear, since few studies that directly compare them have been conducted to date.[53]

Principles and treatment strategies

IT should be started early in the disease process so as to modify the natural progression of the disease, including small airway inflammation. The optimal dose maintenance technique is used in IT, in which as high a dose as possible is delivered without causing unacceptable side effects. An arm reaction that exceeds 25 mm in size is considered an indication of a higher than optimal dose. Doses of 5–20 μg of major allergen per maintenance injection are optimal to most subcutaneous allergen vaccines, whereas the total required dose in SLIT is typically 50–100 times the cumulative dose of SCIT.

The symptoms of the patient determine the duration of the treatment. Complete withdrawal of treatment may be considered if the patient remains symptom free for at least one year. However, it is recommended that patients should have two to three years of reduced symptoms or symptom-free periods, and three to five years of treatment to achieve effective lasting benefits.

Risks and side effects

Systemic reactions with SCIT occur in 2%–3.7% of patients,[54,55] although severe reactions have been reported to be as high as 5.2% in one series.[56] Death by injections has been estimated to be as low as 0.00007% of injections (US Food and Drug Administration estimate). The rate of adverse events in SLIT has been reported to be 17%–60%.[42] The majority of these side effects are local (oral itching or swelling) or gastrointestinal upset. Systemic reactions, which include asthma and anaphylaxis, although uncommon, have been reported. No fatal events have been reported in any study.

Children and pregnancy

It is generally recommended to start IT after the age of five, as the benefits of specific IT below the age of five require further evaluation.[24] However, a recent study conducted by Rolinck-Werninghaus et al has proven the efficacy of SLIT in children aged 3–14 years, although the results were analysed as a whole and no subgroup analysis were performed for subjects below the age of five.[57] This study, together with several post-marketing surveys, has shown that SLIT is relatively safe in children.[58,59] Few studies have been performed for SCIT in children less than five years of age to establish its safety profile in this age group. For this reason, coupled with the fact that compliance is more likely due to avoidance of injection, SLIT is favoured over SCIT in children.

Pregnancy is not a contraindication to IT, and each case should be considered individually. Patients who have already been commenced on IT in the maintenance phase should continue the treatment; however, it is not recommended to initiate IT or to increase the dose during pregnancy.[60]

ROLE OF SURGERY

In some cases, the symptoms of AR (e.g. obstruction, anosmia) may be compounded by a structural element. These include inferior turbinate hypertrophy and deviated nasal septum, and may be improved with surgery. However, the majority of cases of AR can be managed medically.

CONCLUSION

AR is a common condition in Singapore and can be a disease of considerable morbidity. Differentiating AR from other forms of rhinitis and chronic sinusitis is important, since the management of each condition is different. Management includes education and environmental control, as well as various pharmaceutical therapies. The choice of pharmaceutical therapy should be based on the severity, nature and chronology of the symptoms. IT is an emerging modality of treatment that has been proven to be safe and effective, with high levels of evidence available in the treatment of both rhinitis and asthma. Employing evidence-based treatment of AR enables optimal management with adequate control of the condition in most cases.

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SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME
Multiple Choice Questions (Code SMJ 201007B)

	True	False
Question 1. Allergic rhinitis:		
(a) Has a local prevalence of 40% in Singaporean school children.	☐	☐
(b) Can occur at any age.	☐	☐
(c) Is more common in females.	☐	☐
(d) Does not affect the quality of life.	☐	☐
Question 2. Allergic rhinitis:		
(a) Has an early and a late phase reaction.	☐	☐
(b) Is immunologically mediated.	☐	☐
(c) Is associated with asthma.	☐	☐
(d) Can coexist with rhinosinusits.	☐	☐
Question 3. The following is a symptom of allergic rhinitis:		
(a) Watery rhinorrhoea.	☐	☐
(b) Facial pain.	☐	☐
(c) Sneezing.	☐	☐
(d) Itchy nose.	☐	☐
Question 4. Management of allergic rhinitis includes:		
(a) Antibiotics.	☐	☐
(b) Identification and avoidance of the offending allergen.	☐	☐
(c) Steam inhalation.	☐	☐
(d) Nasal steroids.	☐	☐
Question 5. Concerning immunotherapy:		
(a) It is the first-line treatment for allergic rhinitis.	☐	☐
(b) It can be delivered subcutaneously or sublingually.	☐	☐
(c) It can be administered and completed within weeks.	☐	☐
(d) It is without any associated risk.	☐	☐

Doctor's particulars:

Name in full: _____

MCR number: _____ Specialty: _____

Email address: _____

SUBMISSION INSTRUCTIONS:
(1) Log on at the SMJ website: http://www.sma.org.sg/cme/smj and select the appropriate set of questions. (2) Select your answers and provide your name, email address and MCR number. Click on "Submit answers" to submit.

RESULTS:
(1) Answers will be published in the SMJ September 2010 issue. (2) The MCR numbers of successful candidates will be posted online at www.sma.org.sg/cme/smj by 20 September 2010. (3) All online submissions will receive an automatic email acknowledgment. (4) Passing mark is 60%. No mark will be deducted for incorrect answers. (5) The SMJ editorial office will submit the list of successful candidates to the Singapore Medical Council.

Deadline for submission: (July 2010 SMJ 3B CME programme): 12 noon, 13 September 2010.