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Council Members

Editorial Board

Message from the Immediate Past President

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The pandemic is still raging on. No one is immune from the threat of this novel coronavirus including elites and world leaders. 2020 is proved to be a challenging year by all dimensions socioeconomically and geopolitically. We are so proud of Hong Kong people who have been very disciplined collectively in keeping the COVID-19 at the lowest possible rate. It is something the rest of the world is envy about and wanted to learn from. 8-9 months long battling against the pandemic we have claimed one victory after another through good civic citizenship and good science. The recent good turn-out of 1.8 million citizens orderly participated the Universal Community Testing under the staunch support of Central Government and volunteering of many devoted health care professionals which is a showcase. It shouts out loud to the rest of the world that HK is backing on its feet and heading out to the right path. I hope such scheme may reassure more people that it is perhaps about the time that we can gingerly resume some of our business and activities, though we should keep our high vigilance because there is still a long way to come over this pandemic.

Despite all the uncertainty, HKIA has taken on the challenges and tried best effort to deliver our duties and responsibilities. Making sure the needs of allergy communities are not overlooked is one of our key roles during this pandemic. We continued to provide quality professional education and training programmes, patient support and public engagement though our collective resolution, flexibility, and adaptability. We witnessed a dramatic decline or delaying in seeking elective medical consultation in the last few months. At the same time, there is an upsurge of eczema, contact and chemical hypersensitivities in the community. We empathised the allergy community that many of their health needs remain unmet. We strived better ways to address them. Tele-consult is becoming a new norm and may stay in for a longer term. At the Council level, we continue to support our members with the best research offer seed money to young researchers. Like many organisations, we are now working and meeting remotely.

HKAC 2020 postponement

The theme for HKAC 2020 was confirmed as “Novel Diagnostics and Therapy for Allergy and Asthma”. It was suggested to have a 2-day programme for HKAC 2020, and parallel sessions for Allied Health and ENT were recommended. The venue was chosen as usual HKECC. The OC finally decided to postpone it to next year. Instead, a 1-day ASM was in lieu with. COVID -19 and Allergy is the theme. I am grateful to Professor Gary Wong, Dr. Tak Lee, Dr. Chris Lai and many others have crafted a compact and stimulating programme for us and our colleagues. We have the top notched COVID 19 researchers and clinical leaders to join us. We have the most talented academic allergists to reveal the best insights of HK. I also thank all the sponsors for their endurance and generosity at this extraordinarily difficult time.

Research grant application

It was led by Professor Gary Wong and a panel of reviewers. A total of 8 applications were received before the deadline. Council members agreed to increase the grant to HK$300,000 this round in view of positive responses. Eventually, 4 well deserved study proposal were awarded with either partial or full funding. It was concluded that applicants who were junior researchers should have bonus points in the assessment of the research grant application, as it is considered as seeding money to encourage them in embarking on allergy related clinical or basic research.

Public engagement

Joint Press Conference with the Hong Kong Allergy Association (HKAA) was successfully held on 27 June 2020 (Saturday) going in line with the World Allergy Week 2020. The focus of this press conference was on anaphylaxis care and prevention. Dr. Phil Lee has organized the patient interview by press and presented the up-to-date local research data. It was widely covered a media.

Originated by the idea from Dr. Tak Lee for better public/patient engagement, HKIA has formed a new patient engagement working group in collaborations with Allergy Hong Kong. The first meeting was held on 16 December 2019 (Monday). A project on severe allergy registry was conceived and currently in active pursuit. It will devolve into education campaign for nurseries, schools, restaurants and hotels. It capitalizes on the current partnership and forges new momentum to deepen our understanding of immediate allergy at the community and preach for proper pre-hospital management. HKIA will provide academic supervision and finance governance.

A recent eczema quality of life survey was completed and released to public with the help of Dr CK Yeung and a psychiatrist. It is disheartening to learn many eczema patients have depression and suicidal ideation because of their poorly controlled eczema. Much more work awaits us to get around with it.

Membership

It was updated that HKIA currently had 418 ordinary members and 438 associate members, making up a total of 856 members. HKIA is very pleased to announce it has received a grant from AstraZeneca Hong Kong Ltd., Mundipharma (Hong Kong) Ltd., and Stallergens to support the registration fee for 90 new ordinary members (200 each) and 270 new associate members (100 each) to join HKIA. In addition, the Council of HKIA has decided to waive annual dues from all members effective immediately until further notice. Coupled with a progressive and comprehensive strategy to grow the discipline, there has never been a better time to join HKIA to support your colleagues, so please spread the news!

Conference sponsorship and scholarship

The conference sponsorship for local and overseas conference would normally be announced for application in July. It was discussed and concluded that the announcement would not be sent out at this stage due to the COVID-19. It was suggested to defer the announcement to quarter four of 2020. If attending overseas conferences were still not possible by then, the sponsorship could be used for supporting members to join the ASM 2020.

Education, and training

Allergy certificate course with FMSHK

It was led by Dr. Alson Chan and we have had another successful run this year but on-line, with one lecture every Thursday for 6 weeks, scheduling on 2, 9, 16, 23, 30 July and 6 August 2020 (Thursday). It has expanded the attendance by two-fold with over 200 doctors, nurses and allied and health professionals attended and earned their CME/CNE/CPD marks. The feedback survey was overwhelmingly positive, and very likely we will make it a yearly event whether physically or virtually, if FMSHK continues to invite HKIA to be the provider.

Multi-specialty medical mega conference 2020

HKIA has supported M3C as a co-organizer, which also has postponed from 25 - 26 April 2020 to 12 September 2020 and switched from physical to a virtual online programme. 'A basket of allergies' was chaired by Professor Ellis Hon, co-chaired by Dr. Ludwig Tsoi from emergency medicine society. It was a nice cross over and well attended event.

Publication

Newsletter

HKIA e-Newsletter was successfully published consecutively despite the difficulties during the pandemic and the political unrest. I am indebted to Chief Editor Dr. Jaime S.D. Rosa Duque and his team. With the nomination from Chief Editor and endorsement from the Council, a few doctors had accepted to be the Associate Editor / Subeditor: Dr. Jason YK Chan from The Chinese University of Hong Kong/Prince of Wales; Dr. David Luk from United Christian Hospital for Skin Allergy section for the future; Ms. Chara Yip from Queen Mary Hospital as subeditor for the HKIA e-newsletter's Allied Health Professional section. The authorship would be expanded to non-clinical scientists from the pharmaceutical and biotechnology industries. The content of the e-Newsletter now is more relevant to daily clinical practice. Some articles would be written from the patients' perspective. Ms. June Chan also invented a corner of "Ask the Expert", which enhances the readability to allied health professionals and public. We welcome them and are grateful for bringing the newly formatted Newsletter to a greater audience.

HKIA-HKEC harmonisation of adrenaline autoinjector prescription

The respective organizations have nominated a panel experts, which formed the anaphylaxis alliance steering committee. Through questionnaires, data analysis, deliberation, and harmonization process among the members, a consensus statement was reached. The manuscript has completed and submitted to HKMJ for publication. I am grateful to Dr. Philip Li for his idea and dedication to execute and Dr. Axel Siu, President of Emergency Medicine College for facilitation.

Social

With social unrest and social distancing over the last 12 months, we have no choice but to defer all our plans. Our vivid memories stayed in the last event that Dr. Alfred Tam and Ms Vivian Lau had organised a wine tasting in conjunction faculty dinner of last ASM. We look forward to the next occasion that we can have face-to-face social events.

Relationship with industrial partners

HKIA has resolved to embrace increasing transparency and accountability for our projects to members and public. It was proposed by Dr. Tak Lee to review the relationship with industrial partners. It was raised that there was tension of over-marketing from the industries while HKIA should play a role by providing good advice and take note on the conflict of interest on the collaboration with industrial partners. A consensus practice guideline was drafted by Dr. Lee, endorsed by the Council and uploaded onto the website. The Council Members also need to declare their conflict of interest upon relevant issues.

Danone Nutricia agreed to be the Gold Sponsor with sponsorship of HK$300,000 per year for two years (i.e. HK$600,000 for 2 years in 2019 - 2021) to support the educational activities organized by HKIA. We vowed to make sure every dollar is well spent for the purpose of training and education.

Switching presidency and office-bearers and council members

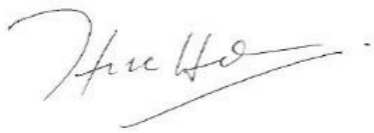
There would be nominations of new office-bearers and council members in 2020 AGM. President-elect Professor Gary Wong will preside HKIA in the coming 4 years. We all have high hopes that Professor Wong, with his international scholar calibre and vast networks, will lead HKIA to navigate through the murky pandemic time and scale new heights. Council members who served for 4 years would step down. Professor Ellis Hon has agreed to continue to serve as our Advisor. I am particularly grateful to Advisor Professor Henry Chan and Honorary Treasurer Dr. Alice Ho for their unfailing support and most trustworthy advice during my tenure. Professor Chan cannot continue as our Advisor due to personal reasons. We bid a fond farewell to him and wish him all the best in his future endeavours. Dr. Alice HO will step down as Honorary Treasurer. We are indebted to her leadership, capable financial prudence and prowess that HKIA has a sustainable financial status, which is so important that we can strive for our goals for common good.

A concluding remark

This has been a very disruptive period, and I want to thank you for your patience and understanding in dealing with any postponement, alterations or cancellations. I owe a huge THANK YOU to all my councils, in particular Office Bearers Dr. Helen Chan, Dr. Tak Lee, Professor TF Leung and Dr. Alice Ho for their candid advices, suggestions, actions and counsel. I would like to express my high admiration to the efficient works of MIMS and ICC's Secretariat. I am glad that despite the idling society by and large, many exciting developments are pushing forward inch by inch out of many people's goodwill within HKIA and from outside.

I also want to send a message of my appreciate for the solidarity displayed by our colleagues in Mainland China. We have witnessed their unparalleled efficiency in locking down the amplification epicentre Wuhan and the surrounding cities, their courageous combat against the virus-stricken crises and to cure a tsunami of critical patients. Through such hard work, they have now earned their first round of victory. They have warned and bought time for the world. They have worked tirelessly to share their experiences by many superb quality research outputs. We thank them wholeheartedly for their outstanding work in the recent HK Universal Community Testing project.

Finally, I am stepping down with a wealth of knowledge I will always treasure. Working with the amazing colleagues of HKIA has been a fantastic learning experience. I feel as if being here with you all each day has made me a more well-rounded person. I have learned to be open-minded, to value other people's opinions and to consider other ideas along with mine, to end up with a great result. I have full confidence HKIA will grow from strength to strength under Professor Gary Wong's leadership. I wish the new Council every success in its future endeavours. I wish every member of HKIA and the wider allergy community good health and good luck!



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Message from the Editors

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This past year has included many ups and downs, from politics to waves of high incidences of the deadly coronavirus. Bless you all and I wish everyone a healthy rest of this year. I urge you all to continue to protect yourselves and your wellbeing with the upcoming onslaught of ongoing coronavirus, winter season which is usually accompanied by many other viruses including the flu and election time. For some of you, I hope that there have been some advances in telehealth so that you will be able to take care of patients while maintaining optimal social distancing. On the positive note, I thank and congratulate HKIA's Organizing Committee for the arrangement of an incredibly attractive Annual Scientific Meeting 2020, which will air as a virtual meeting on 11 October 2020! The program is absolutely sensational, and we are all looking forward to conferring for all the interesting talks as planned!

This message to you marks another issue of the HKIA e-newsletter. Our editorial team expresses our genuine appreciation to all subeditors and authors to help us keep up to date on the latest clinical practice and research progress relevant to our allergy practices despite the recent social and health-related pressures. Thank you all so much for your hard work during these difficult times!

There are several updates in this issue. First, we thank Dr. Marco Ho for the many successes he achieved for us as our HKIA president the past few years. Amongst the many triumphs, the HKIA e-Newsletter has certainly improved considerably because of his tireless contributions and support. Thank you very much, President Marco Ho! With that said, we are very excited to welcome Professor Gary Wong as he becomes our new HKIA president. Professor Gary Wong is a well-respected and accomplished physician scientist in the field of allergy who will certainly continue to raise HKIA to new heights!

Secondly, thanks to the important addition of Dr. Allie Lee, Assistant Professor of the Department of Ophthalmology at the University of Hong Kong, into our group, we have launched the new section, Eye Allergy. Dr. Allie Lee has kindly pledged to offer her expert perspectives and advice to the Eye Allergy section and allergic ophthalmologic disorders for HKIA regularly, and therefore we are very happy that Dr. Allie Lee has accepted to be the subeditor of this new HKIA e-Newsletter section. She commences by giving us a basic overview on allergic conjunctivitis. Many thanks to Dr. Allie Lee and we welcome you to the HKIA family!

Due to the huge concerns related to COVID-19 itself and also how it may affect our allergy practice, this issue of the HKIA e-Newsletter continues to include articles related to this disease and its associated outbreak. We hope that by keeping COVID-19 in our discussion, together we can come up with more solutions to optimize our allergy services while dealing with this highly infectious and deadly pathogen.

With that said, our subeditors and contributing authors certainly feel that COVID-19 is important to all of us, so much so that 2 respiratory medicine specialists—Dr. Veronica Chan and Dr. Alice Ho—and a paediatric immunologist, allergist and infectious disease specialist—Dr. Polly Ho—all wrote on the topic of the implication of COVID-19 on our asthmatic patients! Do not miss these articles, as there are 3 experts who have important messages for us on this one, single topic! For the remainder of the sinopulmonary tract, rhinitis and sinusitis continue to predominate as the major focus. Dr. Birgitta Wong extends on the topic of dupilumab for the treatment of chronic rhinosinusitis, which was discussed by Dr. Jason Chan in the previous issue, by giving her review and own perspectives on the decision-making process for the use of this novel biologic as opposed to endoscopy sinus surgery. However, some cases of rhinitis are not that severe, and in such lower degrees of inflammation, Dr. Jason Chan provides evidence on the choice of antihistamines. This important ENT topic is complemented by detailed clarification on the appropriate use and dosing of the different topical intranasal sprays by our pharmacist colleagues, Mr. Nath Chu and Mr. Andrew Li.

In addition to Dr. Allie Lee, Dr. Jason Chan, Mr. Nath Chu and Mr. Andrew Li's overviews of the first-line treatment options for allergic disorders in their respective anatomical areas of expertise, Dr. Christina Wong has kindly provided us a similar discussion for the skin. Keeping in line on the fundamentals, Ms. June Chan interviews Dr. Alson Chan as they share the most common manifestation and treatment approach for allergies caused by aeroallergens.

The remainder of this e-Newsletter is a bit of a mixed bag to ensure we offer you a diversity of topics within our field. Dr. Tak Lee, who initiated a discussion on the practical aspects of telehealth use, concludes with his experiences and recommendations in this issue. On the other hand, as a first-hand witness of Dr. Elaine Au's outstanding work on improving the availability of innovative assay technologies in her Clinical Immunology Laboratory, I am very excited for her to present to you her article that describes the latest diagnostic tests that she can run for us within our local hospital system. Then, as Dr. Agnes Leung delineates recognition and management of anaphylaxis, she and Dr. Alson Chan give us hope that immunotherapy is on the horizon, which can hopefully reduce poor clinical outcomes and improve the quality of life for patients with severe allergies. Finally, I advocate for more routine penicillin allergy testing for delabelling patients who do not actually have drug allergies. This approach reduces overuse of alternative antimicrobials, which can be less efficacious than the first-line medication, can have more side effects, can be less conveniently administered, and in the article that I reviewed, can be more costly.

All the articles in this issue were well prepared and written, so I am sure you will all enjoy this issue very much!

Again, please be sure to take good care of yourselves this upcoming winter season. We must all consider receiving the vaccines whenever they first become available! During this time, we hope that this issue of the HKIA e-Newsletter will be helpful to you and your patients.

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Managing asthma during the COVID-19 pandemic: what do we know so far?

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Introduction

The novel coronavirus disease (COVID-19) caused by the new coronavirus (severe acute respiratory syndrome coronavirus 2; SARS-CoV-2) has rapidly spread across the globe, causing up more than 24,000,000 confirmed cases and more than 820,000 deaths.[1] The infection has a wide degree of presentations, from asymptomatic or very mild to severe. A significant percentage of patients develop acute respiratory distress syndrome (ARDS) and even death. Old age and underlying morbidities, such as cardiovascular diseases (in particular hypertension) and metabolic disorders (obesity and diabetes), have been identified as significant risk factors for COVID-19 morbidity and mortality.[2] Viral infections are well known to cause exacerbation in patients with asthma. Would patients with asthma have increased risk for COVID-19 or having poorer outcome? How should we manage asthma during the pandemic? This article aims to address these questions, based on the currently available evidence and guidelines.

Pathophysiology of COVID-19

COVID-19 is transmitted via respiratory droplets or aerosolized droplets. SARS-CoV-2 binds mainly to angiotensin converting enzyme (ACE2) receptors in host cells which are abundant in the lungs, heart, blood vessels and intestine. For about 20% of the infected patients, the disease will progress to pneumonia through propagation of SARS-CoV-2 within type II cells via ACE2 and will compromise the alveolo-capillary space. It may result in a diffuse alveolar damage and fibrosis. A hyperinflammatory syndrome, called 'cytokine storm', consisting of fever, cytopenias, hyperferritinemia, diffuse alveolar damage and hypercytokinemia may occur during this phase, leading to multiorgan failure and a high rate of mortality.

Impact of COVID-19 to patients with asthma

Viral infections, such as rhinovirus, respiratory syncytial virus, influenza virus and human metapneumovirus, are well known to cause exacerbation in patients with asthma. However, for the moment, there is no strong evidence supporting that patients with asthma were at a higher risk of being infected or becoming severely ill with SARS-CoV-2.[3] Most early epidemiologic studies of the COVID-19 pandemic in China and Europe had shown relative low prevalence rate of asthma, ranging from 0.9-4%, which is much lower than the asthma prevalence in the general population.[4-6] Recent reports from the USA and the UK suggest that asthma is more common in children and adults with COVID-19 than previously reported, with prevalence rates ranging from 9.0%[7] - 14.0%.[8] One UK study also identified asthma as a significant risk factor of death from COVID-19, especially in those who recently received systemic steroid.[9] But unlike comorbidities like hypertension, diabetes and severe obesity, asthma was not identified as an *independent* risk factor for increased severity nor worse outcomes.

Would the patients with asthma develop more severe pneumonia or respiratory complications after infection by SARS-CoV-2? A recent study that assessed patients with asthma hospitalized for SARS-CoV-2 pneumonia demonstrated no difference between patients with or without asthma in terms of severity (length of stay, maximal oxygen flow needed, noninvasive ventilation requirement, and intensive care unit transfer). Moreover, SARS-CoV-2 pneumonia did not induce severe asthma exacerbation.[10]

Several hypotheses had been raised for the apparent no increase risk in patients with asthma for COVID-19, in contrast to other respiratory viruses. Firstly, SARS-CoV-2 uses ACE2 as its cellular receptor, and reduced expression of ACE2 in nasal and bronchial epithelial cells among patients with high levels of allergic sensitization and asthma might be a potential contributor to reduced COVID-19 severity in patients with Th2 inflammation.[11] Secondly, eosinopenia has been widely reported in patients with COVID-19. Decreasing the number of eosinophils in eosinophilic asthma might be associated with a reduction in severe exacerbation.[9] Thirdly, inhaled corticosteroid, alone or in association with bronchodilators, inhibit human coronavirus-229E replication, partly by inhibiting receptor expression and/or endosomal function and reducing cytokine production (IL-6, IL-8). This observation suggests that these drugs might modulate infection-induced inflammation in the airways.[12]

Asthma attack or COVID-19: How to differentiate?

The most common symptoms of COVID-19 are fever, dry cough, and tiredness. Other symptoms include myalgia, sore throat, diarrhea, loss of taste or smell. Many of the symptoms overlap with those related to exacerbation of asthma. It is very important to differentiate between the two conditions, as inappropriate treatment of either condition carry substantial risk for deleterious consequences. For instance, delaying the diagnosis of COVID-19 and failure to isolate the infected person will cause spread of the disease and deprive the optimal window period for successful treatment. On the other hand, abstinence from systemic steroid during severe asthma exacerbation due to fear for COVID-19 will significantly increase the risk for more severe clinical outcomes.

There are several key points to differentiate between asthma exacerbation and respiratory infections such as COVID-19. Firstly, persistent high fever, which is common in COVID-19, is not a typical symptom of asthma exacerbation. Secondly, myalgia, or body aches and pains, are also not commonly encountered during an asthma exacerbation. Thirdly, respiratory symptoms of cough and shortness of breath during upper respiratory tract infections due to viruses respond very poorly to bronchodilators. Fourthly, typical features of asthma, including wheezing, diurnal symptom variation, and coexisting atopic symptoms of rhinitis, are much less prominent in COVID-19.[13] Patients are advised to constantly monitor their daily symptoms of asthma, and if they develop any features of COVID-19 without asthmatic features, they should seek urgent medical attendance to arrange COVID-19 testing and subsequent management.

Safety concern with asthma medications

Regular use of inhaled corticosteroids (ICS) reduces severe exacerbations of asthma, while the prompt use of systemic corticosteroids (OSC) during an exacerbation reduces the need for hospital admissions, use of bronchodilators and relapses. For patients with severe eosinophilc asthma that is uncontrolled on standard treatment, add-on biologics (anti-IgE or anti-interleukin-5/5R) have been shown to reduce asthma exacerbations and improve symptom control. There is currently no evidence that ICS or biologics for the treatment of asthma suppress a patient's immunity or antiviral defenses.[14] Data from Spain using big data analytics and artificial intelligence through clinical platform had identified 1,006 asthma patients diagnosed with COVID-19, among a cohort of total 71,192 asthma patients. The proportion of patients with asthma using ICS was significantly lower in individuals requiring hospital admission. In addition, a total of 865 patients in the study population were also being treated with biologics, and there is no statistically significant increase in COVID-19 related hospital admission in biologics-treated patients with asthma.

The latest Global Initiative for Asthma (GINA) 2020 guidelines advise patients with asthma to continue taking their prescribed asthma medication, particularly ICS and OCS.[15] Patients with severe asthma should continue biologic therapy and avoid suddenly stopping OCS if prescribed.

Conclusion

COVID-19 has become a global pandemic, overwhelming our healthcare systems and depleting resource stockpiles. New data are emerging daily, rapidly updating our understanding of this novel coronavirus. With currently available evidence, it is crucial that patients with asthma and other allergic diseases such as allergic rhinitis continue to be adherent to their controller medications, from inhaled corticosteroids to biologics, without making any dose adjustments on their own or stopping these medications, which may lead to a higher risk of asthma exacerbation, increased OCS use, and a higher probability of the need for emergency room access or hospitalization. Each patient should follow the general guidelines for personal hygiene, social distancing and face covering in public areas, carefully monitor their asthma symptoms, and always consider prompt arrangement for specific testing for SARS-CoV-2 if there is contact history or possible COVID-19 symptoms arise. Clinicians much be cautious and recognize the differences between hypoxic respiratory failure due to COVID-19 and bronchospasm from asthma. There is a need to carefully balance the need for OCS prescription, and use of nebulizers should be avoided in order to prevent viral spread.

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COVID-19 and asthma

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Clinical presentation of COVID-19

SARS-CoV-2 is a novel virus that causes the COVID-19 disease.[1] A cluster of respiratory tract infections due to COVID-19 was reported in Wuhan, China, an illness that covers a wide range of symptoms and disease severities. The report summarized the clinical information from 72,314 patients with COVID-19 in China.[1] The case-fatality rate of those with mild symptoms (81% with mild pneumonia or no pneumonia) was only 2.3%. A small subgroup of patients with critical ailments included respiratory failure, multiorgan dysfunction and septicemic shock had case-fatality rates of up to 49%.

Siddiqi and colleagues proposed the use of a 3-stage classification to establish a standardized clinical phenotype process for the immediate risk stratification and management of COVID-19.[2] The first stage is early in the infection, which is dominated by a viral response phase in the early days of the disease, e.g., 5-7 days. It is characterised by mild constitutional symptoms, including fever >99.6°F, dry cough, diarrhoea and headache, with laboratory results showing lymphopenia, increased prothrombin time, increased d-dimer and lactose dehydrogenase (LDH). This stage may be the only stage in the mild disease of young adults and children without co-morbidities. The disease then progresses to the second stage in 10-20% of patients, which is the "pulmonary phase," featuring dyspnoea, shortness of breath, hypoxia. Since the affected patients usually have abnormal chest imaging, tests to exclude bacterial infections are essential, e.g., a low to normal procalcitonin level. About 3-5% of patients will progress to the "hyper-inflammation phase," which is characterised by Acute Respiratory Distress Syndrome (ARDS), Systemic Inflammatory Response Syndrome (SIRS) or shock and even cardiac failure. The laboratory findings include elevated inflammatory marker like C-reactive protein (CRP), lactate dehydrogenase (LDH), interleukin-6 (IL-6), d-dimer and ferritin. These patients may progress to respiratory failure requiring intubation and mechanical ventilation.

Are asthma patients at higher risk of COVID-19?

The Center for Disease Control and Prevention suggests that asthmatics are at increased risk for severe illness from COVID-19.[3] However, after reviewing the study results from Wuhan, asthma and respiratory allergy have not been recognized as significant risk factors for severe COVID-19 based on a large series of patients.[4] The authors revealed that the risk factors associated with severe COVID-19 infection include advanced age, hypertension and a high LDH level. SARS-CoV-2 is a novel virus that targets the angiotensin-converting enzyme (*ACE2*) receptors to gain access to the interior of human cells where they can replicate, causing COVID-19.[1] Jia and colleagues illustrated that *ACE2* serves as the SAR-CoV-2 receptor in the respiratory tract.[5] The higher *ACE2* gene expression increases *in vitro* susceptibility to SARS-CoV-2 infection in human airway epithelia.

The Urban Environment and Childhood Asthma cohort followed prospectively a group of high-risk asthmatic children, who were enrolled prenatally based on the histories of the parents and urban dwelling.[6] Asthma prevalence was assessed at 10 years of age, and 318 children had nasal epithelial brushes obtained when they were 11 years old. The allergic sensitization was inversely related to *ACE2* expression in the nasal epithelium irrespective of asthma status. In contrast to asthmatic children with no/minimal allergic sensitization, children with moderate (fold change [FC] = 0.70; P = 4.2E–3) and high allergic sensitization (FC = 0.54; P = 6.4E–5) had a progressively more significant decrease in *ACE2* expression. Besides, *ACE2* expression was inversely associated with type 2 biomarkers, such as the number of positive allergen-specific IgE test results (β coefficient –0.089; P = 3.1E–5), fractional exhaled nitric oxide (β coefficient –0.45; P = 3.4E–3), total IgE level (β coefficient –0.31; P = 5.1E–6), and nasal epithelial expression of IL13 (β coefficient –0.123; P = 8.6E–5). These results imply asthmatic children with high allergic sensitization and lower expression of ACE2 receptors are protective against COVID-19 infection.

In conclusion, it is pivotal to note that early data suggest an increase in asthmatic patients hospitalised for severe COVID-19 infection.[7] Still, the data does not clarify if those patients are allergic asthma or non-allergic asthmatics. Other essential risk factors such as obesity, smoking, diabetes and hypertension should also be identified since all of these are associated with increasing severity of COVID-19 infection.[7] More studies need to be carried out to confirm whether allergic asthma has a protective effect on COVID-19 disease.

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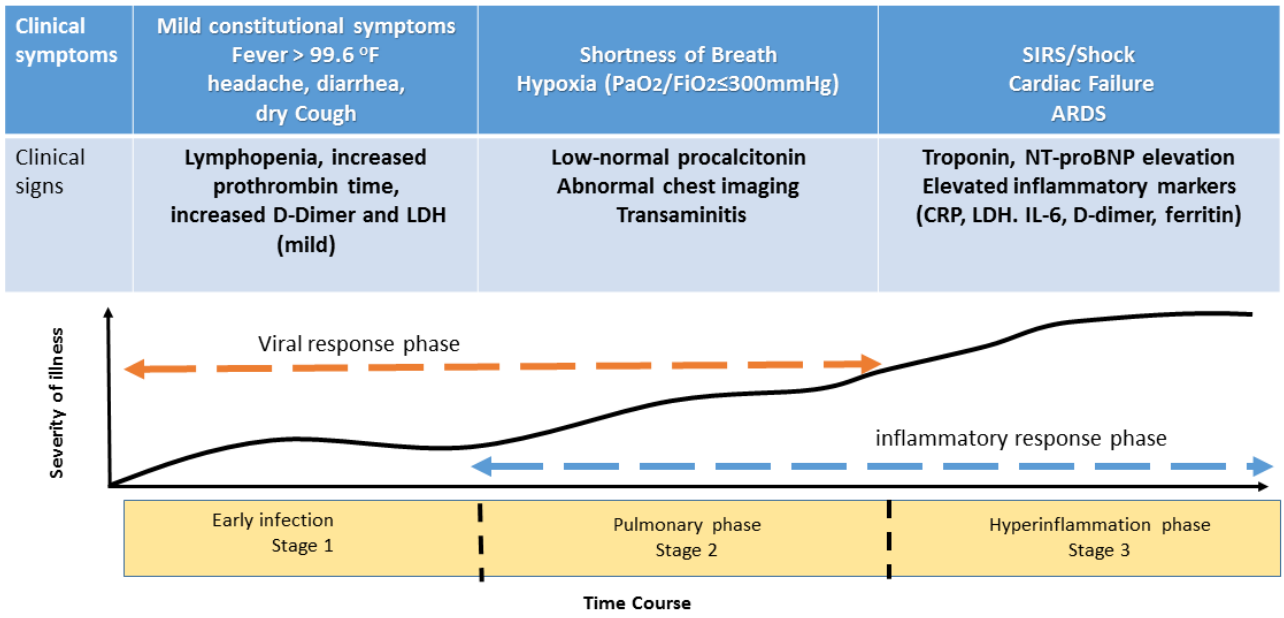
Figure 1. Clinical course of the escalating phases of COVID-19 disease progression.



Intranasal antihistamines in the treatment of allergic rhinitis

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Allergic rhinitis

Allergic rhinitis (AR) is a common chronic disease that significantly affects the quality of life of individuals and their families. AR also has a significant effect on work productivity, days off work and absence from school, resulting in a significant burden on society. Guideline-based treatment algorithms are readily available, in particular the Allergic Rhinitis and its impact on Asthma (ARIA) guidelines which are widely publicized.[1] Despite the availability of these guidelines, treatment of AR remains inadequate for many patients due to a variety of reasons, including the lack of well-defined characterization of AR control, accurate stratification of patients, patient adherence to therapy, patient understanding of the disease and healthcare professional care provision.[2,3]

The mainstay of initial treatment involves the use of intranasal corticosteroid (a separate article in this issue of the e-Newsletter, in the allied health section, discusses the different available intranasal steroids) as a monotherapy that has been shown to be superior to oral H_1 antihistamine or intranasal H_1 antihistamine as monotherapies in the treatment of allergic rhinitis. If monotherapy fails, then combined therapy of intranasal corticosteroid with either route of antihistamine can be used. However, the evidence supporting which combination therapy may be superior or equivalent has been lacking. Here we review an article by Du et al. on the comparison between these combination therapies.[4]

Intranasal corticosteroids with intranasal antihistamine or oral antihistamine?

The meta-analysis by Du et al included randomized control trials that compared combined oral antihistamines with intranasal corticosteroids or intranasal antihistamines with intranasal corticosteroids compared to intranasal corticosteroids alone through an indirect comparison (as there are, to the best of my knowledge, no head-to-head comparisons between the different combinations).[4] A total of thirteen randomized control trials were evaluated for outcomes associated with the quality of life scale Total Nasal Symptom Score (TNSS).

When comparing intranasal corticosteroids with oral antihistamine as a combined therapy to monotherapy there was no significant improvement in TNSS with a combination therapy. On the other hand, when a combinational therapy with intranasal antihistamine and corticosteroid therapy was compared to monotherapy, there was a significant improvement in TNSS with combination therapy. In order to compare the two combination therapies, the authors calculated a relative clinical impact (RCI) for each study. A pooled analysis of the RCI showed that the intranasal antihistamine combination (-58.3%) had a significant improvement in TNSS compared to the oral antihistamine combination (-5%).

Overall, this meta-analysis indicated that intranasal steroids with intranasal antihistamine is superior to the alternative oral antihistamine combination in controlling the symptoms of allergic rhinitis.

Practical aspects of a combination of intranasal steroids and antihistamines for patients

Available to patients in Hong Kong is a combination of fluticasone propionate with azelastine intranasal spray marketed as Dymista for patients 12 years and older. This is available in both the public and private sector in Hong Kong. However, the individual intranasal antihistamine is not available in the public sector. Figure 1 shows that it is recommended for both mild to moderate or moderate to severe allergic rhinitis as a monotherapy based on the ARIA 2019 guidelines. In addition to the superior improvement in symptoms with the combination therapy, the combination has also been shown to have a much more rapid onset of action in improving both nasal and ocular symptoms. [5] The use of a single spray also helps improve compliance as it obviates the need to use two separate sprays, a feat that not many of our patients would like or remember to use. However, patients do need to be warned of a short-lasting, bitter aftertaste, from the intranasal antihistamine component, to ensure that they are compliant with the medication for it to be effective in helping our patients controlling their allergic rhinitis symptoms.

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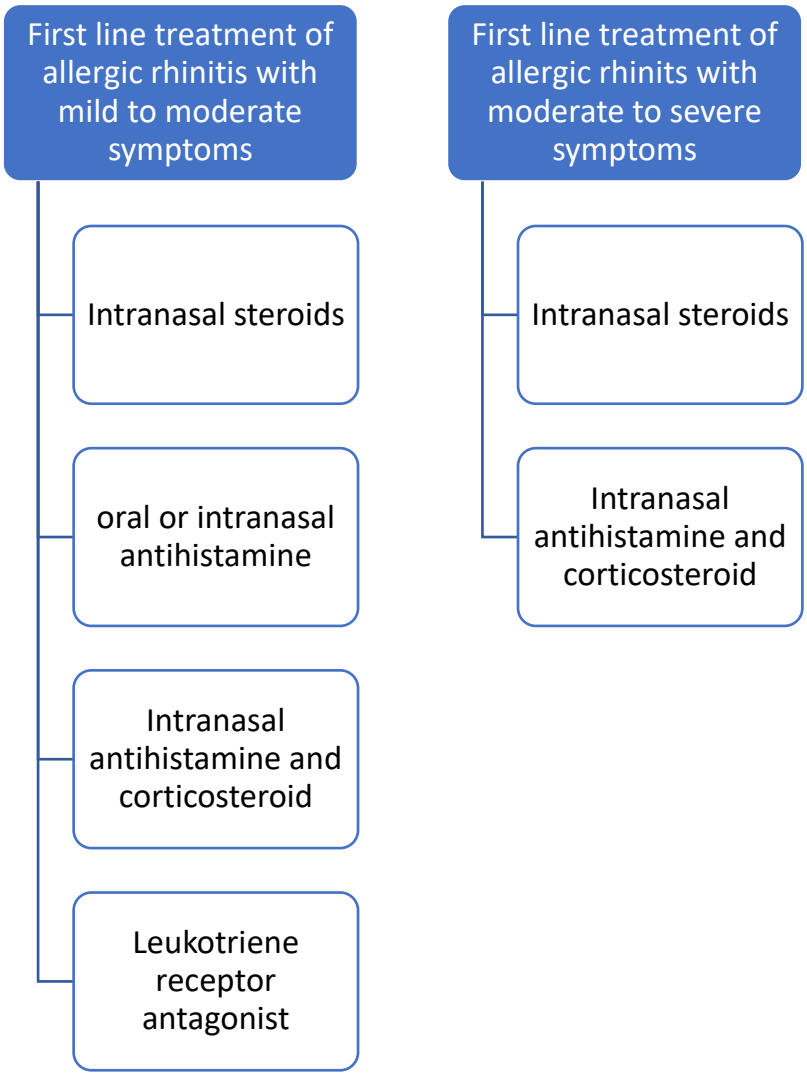
Figure 1. Algorithm for use of therapeutic agents in treating a patient that presents with allergic rhinitis symptoms. The therapies are all as monotherapies and adapted from the ARIA 2019 guidelines.



Decision making in the use of dupilumab versus endoscopic sinus surgery for chronic rhinosinusitis with nasal polyps

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Chronic rhinosinusitis with nasal polyps (CRSwNP) predominantly displays type 2 inflammatory response including IL4, IL5 and IL13 with infiltration of nasal polyps by eosinophils, basophils and mast cells. Patients often undergo endoscopic sinus surgery but there are high rates of disease recurrence, difficult to treat loss of smell, requirement of long-term steroid nasal spray, frequent comorbid late-onset asthma and a poor quality of life.[1-3] Dupilumab is a fully human VelocImmune-derived monoclonal antibody that inhibits signaling by IL4 and IL13. Recently, dupilumab was approved by the FDA as a stand-alone treatment option for adults with CRSwNP. A paper on the phase 3 study was published by Claus Bachert et al in Lancet 2019 on the 'Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (Liberty NP Sinus-24 and Liberty NP Sinus-52): results from two multicentre, randomized, double-blind and placebo-controlled phase 3 trials'.[4] In these 2 trials, efficacy and safety of dupilumab was demonstrated which showed significant improvement in nasal scores, UPSIT scores for smell, Lund-Mackay CT scores and SNOT-22 scores. While dupilumab has shown its promising efficacy in the treatment of CRSwNP, there were more discussions and on-going studies on the decision making in patient selection and cost analysis compared to other treatment modalities and endoscopic sinus surgery. The paper I would like to review is the latest one published in Laryngoscope by George A. Scangas on 'Cost utility analysis of dupilumab versus endoscopic sinus surgery for chronic rhinosinusitis with nasal polyps'.[5]

A cohort of 197 CRSwNP patients who underwent endoscopic sinus surgery (ESS) were compared with a matched cohort of 293 CRSwNP patients from the SINUS-24 and SINUS-52 Phase 3 studies who underwent treatment with dupilumab 300mg every 2 weeks.[4] Utility scores were calculated from SNOT-22 in both cohorts. Decision-tree analysis and a 10-state Markov model utilized event probabilities and primary data to calculate long-term costs and utility. The primary outcome measure was incremental cost per quality-adjusted life year (QALY).

For the results, the ESS costs were $50,436.99 and produced QALY of 9.80 while the dupilumab treatment costs were $536,420.22 and produced QALY of 8.95. An ESS treatment strategy was more cost effective than dupilumab for upfront treatment of CRSwNP. In this study, the number of prior sinus surgeries in the ESS cohort did not impact the results of the cost utility analysis. These findings may suggest that revision ESS should be the preferred option for patients whose polyps and symptoms recur. However, the authors did comment that additional factors need to be considered that are difficult to quantify, such as multiple surgeries involving multiple recovery periods and repeated exposure to general anaesthesia. Revision ESS can be more hazardous, with distorted surgical anatomy and increased risk of complications.[5] The paper has also highlighted the important factors by the European consensus statement in the decision making for initiating monoclonal biologic therapy in CRSwNP patients: 1) evidence of type 2 inflammation, 2) need for systemic steroids in the past 2 years, 3) significant QOL impairment, 4) significant loss of smell, and 5) diagnosis of comorbid asthma. The panel recommended biologics for those with prior ESS if three or more factors are present.

CRSwNP encompasses a heterogeneous group of patients. Selection of treatment options should be a shared decision-making process with detailed discussion with patients, including benefit of revision surgery and extended surgery, unclear duration of dupilumab, possible recurrence of polyps after stopping the biologics as in the study, potential complication of unmasking eosinophilic conditions such as eosinophilic granulomatosis with polyangiitis (EGPA).[4]

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Asthma and COVID-19

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Since the first report of the novel coronavirus in December 2019, the world continues to fight hard against this new pandemic. The medical care of patients with allergic disease never ceases while the relationship between allergic diseases and COVID-19 brought to the attention of many allergists. Here we discuss the current evidence on the relationship of asthma and COVID-19 and its management.

It is well known that respiratory tract viral infections including other non-pandemic human coronavirus can induce asthmatic attack. However, according to data reported in previous coronavirus outbreak as in SARS and MERS, no association was found between these outbreaks and asthmatic attacks. The Center for Disease Control and Prevention reported earlier that patients with moderate to severe asthma are at risk for COVID-19 infection. However in the current COVID-19 pandemic, the reported rates of asthma among laboratory-confirmed COVID-19 patients were variable and generally lower than expected. In earlier studies from China, the rates ranged from 0% to 0.9%.[1,2] The prevalence of asthma was 9% among 5,700 COVID-19 hospitalized patients in a study conducted in the US, which was not significantly higher than the general prevalence.[3] Asthma has not been frequently described in the literature as a major confounder of COVID-19, and asthma is not the top 10 comorbidities according to fatality statistics in New York state in the US. However, a recent nationwide cohort study in Korea found that asthma, especially non-allergic asthma and allergic rhinitis, among all allergic disorders, was associated with worse clinical outcomes of COVID-19 patients.[4] Another recent study from the UK suggested that severe asthma is a risk factor for in-hospital mortality for COVID-19.[5] In the absence of more conclusive evidence, asthma, in particular severe asthma, should be regarded as high risk for COVID-19 infection and its complications.

Besides under-diagnosis or under-reporting being a contributing factor in earlier studies, there are a number of hypotheses that may explain the protective effects of asthma to COVID-19 infection (Table 1). The level of gene expression of angiotensin-converting enzyme 2 (ACE2), which is the cellular receptor for SARS-CoV-2 viral spike protein binding, was found to be lower in patients with asthma. It was shown that ACE2 expression was reduced after exposure to allergen, and allergic sensitization was inversely correlated to nasal epithelium ACE2 expression.[6] However, Sajuthi et al reported findings of upregulation of transmembrane protease serine 2 (TMPRSS2), which plays a crucial role in cleavage of viral protein for virus-host cell membrane fusion and cell entry, by type 2 allergic inflammation mediated by interleukin-13.[7] More convincing evidence on the expression of ACE2 and TMPRSS2 in asthmatic patients are required. Trained immunity in chronically inflamed respiratory tract is postulated to provide anti-viral immunity. Molecules of the innate immunity in the respiratory tract, including mannose-binding lectin and surfactant protein D, have anti-viral functions and were found to have higher concentrations in asthmatic patients due to chronic inflammation. On the other hand, impaired production and a lower level of interferon-gamma (IFN-γ) was found in patients with asthma, thus impairing their anti-viral immunity. However, it may also be favorable in reducing ACE2 expression, which is dependent on IFN-γ production.[7]

There is a theory that due to the chronic and sustained type 2 immune response, including type 2 cytokines, accumulation of eosinophils and inflammation in the respiratory system of patients with asthma, asthma may not be a major risk factor for COVID-19 disease. Experimental studies have shown a potential role of eosinophils in promoting viral clearance and antiviral host defense in other respiratory virus infections. On the other hand, IgE cross-linking, a classical feature of allergic diseases, dampens antiviral immune response through abrogating interferon-alpha (IFN-α) response, and serum IgE level is inversely correlated with IFN-α production.[8] Further studies on the immunity of COVID-19 infection and its relations to allergic responses are required to support a sound conclusion.

There is evidence that pre-existing long-term use of inhaled corticosteroids (ICSs) in asthmatic patients may exert protective effects. Ciclesonide was found to block SARS-CoV-2 replication.[9] Pre-treatment use of budesonide has been shown to inhibit replication of human coronavirus HCoV-229E and cytokine production in the respiratory epithelium in *in vitro* study.[10] The use of ICS was also shown to be associated with a reduction in ACE2 and TMPRSS2 gene expression from sputum in patients with asthma.[11] These results suggested protective effects of ICS use on COVID-19 infection, yet larger studies are required to confirm these preliminary findings.

The management of asthmatic patients became challenging during the pandemic period. It was recommended to advise asthmatic patients to continue taking their ICSs and add on treatments during the pandemic.[12] Optimal control of asthma is believed to be the best protection against a SAR-CoV-2 exacerbation. Due to risk of aerosol generation and infection transmission, use of nebulizers in hospitals and clinics had largely been avoided since start of the pandemic. A risk stratification plan that aims to avoid nebulised therapy, when possible, was proposed.[13] It was recommended to recognize early the severity of asthmatic attack, with early institution of multiple doses of metered-dose inhaler (MDI) treatment via a

spacer with a mouthpiece or a tightly fitted face mask with more rapid initiation of systemic therapy, which may help ensure patients are less likely to deteriorate to the stage where nebulized therapies are required.[12,13] Systemic treatment should be considered early in patients with severe asthmatic attack. In patients with acute respiratory failure or when use of MDI is not feasible, nebulizer therapy with placement of filter is preferred. If the facility allows, this route of administration is preferably performed in a single room with adequate air change per hour.

The use of systemic steroid was found to delay viral clearance in SARS-CoV and MERS-CoV, and therefore routine use was not recommended in these diseases. The evidence for systemic steroid use in COVID-19 is still emerging. WHO recommended against the routine use of systemic steroid for treatment of COVID-19, unless it is indicated for other diseases, as a meta-analysis found that ICSs did not significantly reduce mortality, disease severity and had several adverse effects.[14,15] However, it is essential to control patient's asthmatic attack, while systemic steroid remains as the recommended treatment for severe asthma exacerbations in the current national and international asthma guidelines. The Global Initiative for Asthma recommends continuing the use of oral steroid for asthmatic attack and as indicated in patients with symptoms of bronchoconstriction during the SARS-CoV-2 pandemic.[12] The Canadian Thoracic Society position statement also recommends systemic steroid for the treatment of asthma exacerbations during the SARS-CoV-2 pandemic, whether or not the exacerbation is triggered by SARS-CoV-2.[16]

Out-patient management of patients with asthma had also been affected due to scaling down of elective services and follow up. Consideration for postponing routine follow up for patients with controlled mild asthma can reduce their risk of contracting the infection. It was recommended that clinic follow up of patients with well-controlled asthma and without emergency visit in the past 6-12 months and who have received ≤1 oral steroid in the past 6 months may be postponed or managed via telemedicine service.[17]

The COVID-19 pandemic will likely continue for a period of time until the availability of effective vaccination. The coming winter surge, with the usual peak of seasonal influenza infections and other respiratory virus infections, in the background of COVID-19 pandemic, will pose a big challenge to the management of patients with asthma. Medical care of asthmatic patients should be modified according to the needs of patients, and clinicians should remain updated on the latest evidence and the outbreak situation.

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Table 1. Hypotheses for predisposition or resistance to COVID-19 in asthma patients.

Predisposition	Resistance
Upregulation of transmembrane protease serine 2 (TMPRSS2), which plays a crucial role in cleavage of viral protein for virus-host cell membrane fusion and cell entry, by type 2 allergic inflammation.	Lower level of gene expression of angiotensin-converting enzyme 2 (ACE2), which is the cellular receptor for SARS-CoV-2 viral spike protein binding, in asthma patients.
Impaired production and lower level of interferon-gamma (IFN-γ), which is an important immunity against COVID-19.	Trained immunity in chronically inflamed respiratory tract provides anti-viral immunity. For example, asthmatic patients have higher concentration of mannose-binding lectin and surfactant protein D in respiratory tract.
IgE cross-linking, a classical feature of allergic diseases, dampens antiviral immune response through abrogating interferon-alpha (IFN-α) response, and serum IgE level is inversely correlated with IFN-α production.	Use of inhaled corticosteroids (ICS) in asthmatic patients may be protective. Ciclesonide block SARS-CoV-2 replication. Budesonide inhibit replication of human coronavirus HCoV-229E. Use of ICS is associated with reduced ACE2 and TMPRSS2 gene expression.

Severe allergic conjunctivitis in children: an ophthalmologist's perspective

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Allergic conjunctivitis (AC) occurs frequently in the paediatric population. It was estimated that up to 30% of children with atopic conditions, either rhinitis, asthma or eczema, would have some form of concomitant AC.[1] It is a spectrum of immunological inflammatory process of the ocular surface, including seasonal allergic conjunctivitis (SAC), perennial allergic conjunctivitis (PAC), vernal keratoconjunctivitis (VKC) and atopic keratoconjunctivitis (AKC).[2,3] The clinical and immunological features of the major types of ocular allergic diseases in children are summarized in Table 1.

A majority of patients present with milder forms of AC, namely SAC and PAC. VKC and AKC, on the other hand, are a severe form of disease, pathologically characterized by the late phase of IgE-mediated hypersensitivity. They are potentially sight-threatening due to cornea involvement with ulcers and scarring.[4] Patients usually present with copious discharge and painful visual disturbance, for which prompt referral to an ophthalmologist is necessary.

Ophthalmological diagnosis of the severe forms of ocular allergies is primarily clinical. The classic signs of giant papillae in the palpebral conjunctiva, shield ulcer and vernal plaque on the cornea are shown in Figures 1a and 1b. Topical antihistamines (e.g. emedastine), mast cell stabilizers (e.g. pemirolast) and dual-acting agents (e.g. olopatadine) alone are usually inadequate for control of local symptoms, and therefore a short course of topical corticosteroids is indicated. The topical corticosteroids are usually prescribed by an ophthalmologist because close monitoring for iatrogenic complications, such as glaucoma and cataract, is required.[5] Topical non-steroidal anti-inflammatory drugs (NSAIDs) are rarely used due to their local side effects, in particular burning/stinging sensation that is intolerable to most patients.[6]

In refractory cases of severe VKC and AKC, the use of topical cyclosporin A as steroid-sparing agents has been shown to be effective and has gained popularity in recent years.[7,8] Compounded formulations with concentrations ranging from 0.05 to 2% have been reported from different institutions and a cyclosporine 0.1% cationic emulsion is now commercially available.[9] Tacrolimus eye preparations have been reported to be effective as well, but there are concerns about the frequently reported burning sensation and risk of infections.[6] Systemic immunosuppressants and biologics may be considered in refractory cases.[6] but the evidence available so far is inconclusive and further clinical trials are warranted. In complicated cases, surgical options, including local steroid injection, vernal plaque removal (post-operative photo as shown in Figure 1c) and amniotic membrane transplantation are in the armamentarium of ophthalmologists.

Adjunctive use of some simple measures is often appreciated by patients. Cold compress, for example, can bring quick symptomatic relief. Artificial tears, preferably in the form of a single-dose preservative-free preparation, minimize local toxicities and improve comfort level. Eye gel and ointment, on the contrary, may exacerbate the stickiness experienced by patients due to their high viscosity.

A comprehensive management plan is not complete without psychological care and counselling. Individualized support is important for helping children and their concerned family cope with the debilitation, in particular loss in school days and activities, brought on by the ocular surface disease.

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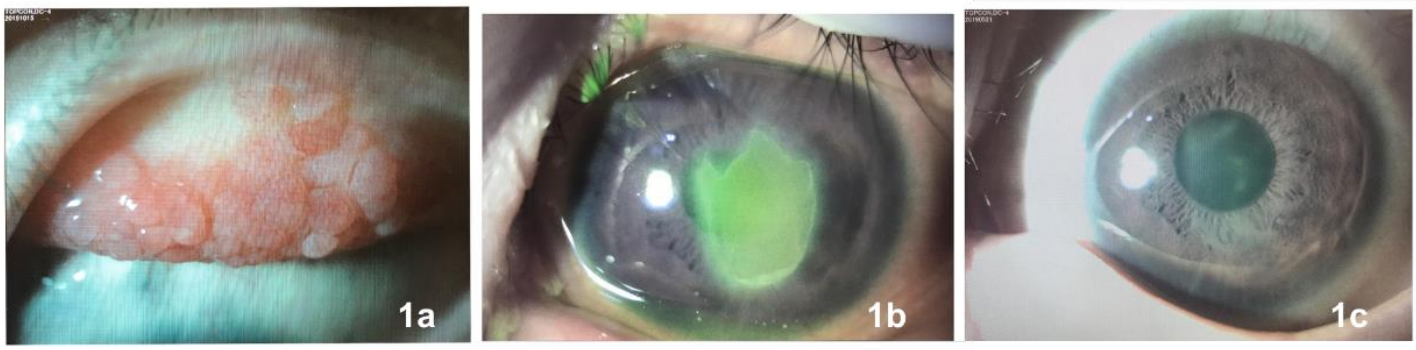
Table 1. Summary of major ocular allergic diseases in children.

	SAC	PAC	VKC	AKC
Presentation	Intermittent (< 4 weeks)	Persistent (>4 weeks)	Chronic and seasonal exacerbations	Chronic
Occurrence	Very frequent	Frequent	Rare	Very rare
Mechanism	IgE-mediated	IgE-mediated	IgE- and non-IgE-mediated	IgE- and non-IgE-mediated
Systemic	Atopic	Atopic	Childhood (<10 years old) Atopic	Adulthood Atopic
Conjunctivitis	Follicles* and/or papillae**	Follicles and/or papillae	Papillae Giant papillae	Papillae Giant papillae
Corneolimbus involvement	No	No	Yes	Yes

SAC, seasonal allergic conjunctivitis; PAC, perennial allergic conjunctivitis; VKC, vernal keratoconjunctivitis; AKC, atopic keratoconjunctivitis.
* *Follicles: avascular collections of lymphocytes; appear as small nodules with a pale surface*
** *Papillae: inflammatory reactions around a central core of vascular channel; sizes vary from small to cobblestone appearance and with a red surface*

Figure 1. Clinical photos of a patient with severe vernal keratoconjunctivitis (VKC), presenting with giant papillae in cobblestone appearance (1a), shield ulcer and vernal plaque in the cornea (1b). The plaque was surgically removed. The ulcer healed with mild scarring and the patient regained good visual acuity (1c).



Peanut oral immunotherapy improves the quality of life for patients and their caretakers in real-world setting

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The prevalence of food allergy is still on the rise in Asia. In China, the prevalence of oral food challenge proven food allergy is around 7% in preschoolers, which is comparable to the reported prevalence in European regions.[1] The recommended treatment for food allergy has been strict allergen avoidance and emergency treatment with rescue medications (e.g. adrenaline) in case of accidental allergen exposure. Unfortunately, strict allergen avoidance can be difficult when eating outside in restaurants or during travels. Besides, food labels in some countries may be misleading. These create significant anxiety in the daily lives of patients with food allergy, which often limits their social interactions and significantly impairs the daily quality of life (QoL) in patients and their caretakers. Therefore, there is an urgent need for food allergy patients to have more effective treatment options to tackle their potentially life-threatening conditions.

The recent approval by US FDA for a peanut oral immunotherapy (OIT) product, Palforzia, can shed more light for patients with peanut allergy. Peanut OIT is one of the most investigated treatment strategy, with multiple research studies supporting its efficacy and safety under appropriate clinical settings.[2,3] Recently, more researchers are also focusing on the changes in QoL for patients undergoing peanut OIT.

A recently published study by Blackman et al is the first to evaluate the changes of QoL in a group of children and adolescent with peanut allergy receiving peanut OIT in real world setting.[4] It recruited an open prospective cohort of 21 patients aged 4 to 17 years receiving peanut OIT using a slow buildup protocol with a median duration of 283 days. The changes in the QoL were assessed using a validated Food Allergy Quality of Life questionnaire. After peanut OIT, there were statistically significant improvements in the overall QoL scores as well as the scores in the subscale of Social & Dietary Limitations and Food Allergy Independent Measure, indicating that the patients and their caretakers had an improved QoL with fewer concerns about accidental exposures, fewer limitations in dietary choices, and fewer disturbances in social interactions.

The limitations of the above study are the use of less rigorous OIT protocol allowing minor individual adjustment in their follow-up schedules, lack of a control group, a small sample size and a single academic centre which may not be representative for general populations from community settings. But the findings of this study are consistent with several other OIT studies focusing on QoL. A randomized controlled trial of peanut OIT in 99 UK children showed significant QoL improvement after successful desensitization.[5] Blumchen et al. reported significant improvement in QoL of 62 children undergoing low-dose peanut OIT in a multicenter, double-blind, randomized placebo-controlled trial.[6] Epstein-Rigbi et al. showed that the QoL of 119 children with food allergy improved significantly upon reaching OIT maintenance phase, with additional improvements noted after 6 more months of treatment.[7] The caregivers' QoL were also improved in a trial of multi-allergen food OIT.[8] Besides, the QoL for patients in Hong Kong were also improved after peanut OIT in a local case series.[9]

QoL represents an important patient-centered outcome of therapy. The treatment goal for our patients should always be holistic with the consideration of QoL for both the patients as well as their caretakers and family members. More studies are now underway to assess in further details regarding the changes in QoL for patients who underwent OIT for peanut and other food allergens. However, in order to measure QoL in a more systematic and consistent way, a standardized outcome measure developed specifically in controlled trial settings to assess the clinic benefit after food OIT is currently in need.

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Telemedicine update

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As promised, I am providing a follow up of my article about telemedicine that was published in the previous newsletter.

The world has been changed by the Covid-19 pandemic and none more so than in our practice of telemedicine. Among telemedicine platforms used in the clinical care sector, Teladoc reported that doctors' virtual consultations have increased by 60% in the first quarter of 2020. A third of sites have said that they are using teleconsultation "a lot."

While I don't have any figures for the use of telemedicine in Hong Kong (HK), I suspect that it follows a similar trend. In fact, there is a longstanding association in Hong Kong dedicated to telemedicine (www.hktelemed.org). The biggest challenge to the use of telemedicine according to a survey by CenterWatch is getting patients to accept it, but once tried, patients find it convenient and safer during the pandemic. Trust and the patient-doctor interrelationship can be an issue, which is the main reason why the Allergy Centre at HKSH only conducts teleconsultations with follow-up patients.

Nearly three quarters of sites in a recent CentreWatch survey also reported that they planned to continue using telemedicine after the pandemic is over, versus about 10% prior to the pandemic, having been convinced of the value of the technology.

In the last 5 months, we have conducted 44 video teleconsultations, of which 19, 18, 4 and 3 were from mainland China, HK, Macau and Canada, respectively.

I raised some questions in my previous article which I have tried to answer below based on our experience:

1) Imperative to correctly identify the person at the end of the phone or video.
As we only conduct video teleconsultations with follow-up patients, we already know them. Nonetheless, we routinely request to check their identification information. If there is an accompanying person in the teleconsultation, it is essential to ascertain in what capacity he/she is there for and to check his/her identification information too.

2) How to ensure confidentiality?
It is imperative to use a secure platform and we initially used WebEx. However we found the video images were less clear than Zoom and connections with the mainland were not always reliable, so we now use the latter platform. WebEx was suggested previously to be more secure than Zoom, but Zoom has since tightened up on its security and this is no longer an issue. The video teleconsultations are all recorded and stored in a secure facility.

3) How to preserve the doctor/patient trust and relationship?
The video teleconsultations should be no different from a direct face to face interview. In our situation, all our patients have already been seen at least once previously in the Centre, so there is an existing relationship.

4) New or old patients or both?
For reasons explained above, we only conduct teleconsultations with follow-up patients.

5) Do you accept overseas/mainland China/Macau residents as patients by telemedicine, bearing in mind that many of us do not have license to practice in some of these jurisdictions?
We conduct virtual consultations irrespective of their location as necessary. Every doctor should confirm with their respective defence union about insurance protection.

With the MPS, the advice is

1. Members must be identifiable by the patient, and comply with any applicable legal or regulatory guidance including any requirement as to identification.
2. Members must only practice within clinical areas in which they can demonstrate appropriate experience and expertise.
3. Members must ensure that they obtain, and can evidence, valid consent from patients.
4. Members must retain full and legible records of all consultations and comply with all applicable laws or regulations.
5. Where members are required to make or confirm a diagnosis, they must ensure they are able carry out an appropriate assessment, including an appropriate history, obtaining and viewing any image or other data which would ordinarily be considered as part of a full consultation. Members should not proceed with a consultation where the remote nature of the consultation or technical limitations (e.g. poor image quality) place limitations on the availability or accessibility of full relevant information. This is particularly relevant to the initial consultation, either with a new patient or in relation to a new clinical condition. MPS would expect members to be able to evidence their reasons for concluding that the consultation was suitable to be undertaken remotely and to record those reasons appropriately in the patient's records.
6. MPS indemnity does not extend to providing cover cross border telephone and video consultations. But during the pandemic doctors

can see overseas patients, but need to document that he is doing it because of quarantine restrictions.

7. If the patient is not able to access local medical advice and you are satisfied that this is the case and documented it as such, you will be able to request assistance from MPS from incidents arising from the consultation, where the complaints or claims are brought in the jurisdiction in which you hold your membership.
8. MPS membership does not extend to providing assistance or indemnity to any third party, or to matters arising from inadequate or faulty equipment.

6) What do the defence unions say about telemedicine? Are you covered by your insurance?

See the above answer, but it is imperative that you confirm with your own defence union. Do not take my word for it!

7) What to do about clinical examination and procedures?

Many clinical allergies, especially cutaneous allergies, can be identified by teleconsultation. However, in all cases, if there is any doubt that the clinical signs cannot be clearly seen or the diagnosis can only be reached by further investigation(s), the teleconsultation should be ended politely and the patient invited to attend in person.

8) What to do about investigations and collection of samples?

Please see my answer above.

9) How does the patient pay if being seen in the private sector? Do you pay before or after the consultation?

When a patient requests a teleconsultation with the doctor or dietitian at the Allergy Centre, a payment link (via paydollars website) is created and sent by email to the patient attaching a consent agreement to be signed. A deadline for payment is provided.

As a condition for completion of payment, the patient agrees that he/she understands and agrees to the following:

a.) Attached Terms and Conditions;

b.) A Personal Information Collection Statement;

c.) If the patient is under 16 years old, a guardian (who must be at least 21 years old) must be present during the telemedicine session. The guardian must show his/her valid identity card to the doctor at the start of the teleconsultation; and

d.) The patient is fully aware of the telemedicine nature and its limitations.

When payment has been made, paydollar.com send a notification that payment has been received, at which point the teleconsultation will be scheduled and the patient informed including a link on how to access the telemedicine session.

On the date of teleconsultation, the staff will login to Zoom 5 mins before the scheduled appointment to confirm the patient's identity. Then, the doctor or dietitian starts the teleconsultation (with video recording).

10) How to prescribe medicines and how to deliver them to patients?

Medication is prescribed after the telemedicine session (if needed) and payment is made online at a website link.

After payment patients or designated representatives can come to HKSH Outpatients Pharmacy with the appropriate identification document to collect medications. If this is not possible or undesirable, the patient will need to arrange an alternative means to collect either the medicine or a prescription to be filled outside the hospital. If the patient lives outside of HK, delivery of medicines to them can be a problem, but in our experience, patients often have very creative solutions.

In every crisis, there is an opportunity and I suggest that an opportunity has arisen to introduce innovation during these extraordinary times; telemedicine is here to stay.

Anaphylaxis – recognizing and responding

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Early recognition is the key

Anaphylaxis is a serious, life-threatening systemic hypersensitivity reaction that is rapid in onset and potentially fatal.[1] In 2006, the National Institute of Allergy and Infectious Disease and Food Allergy and Anaphylaxis Network (NIAID/FAAN) established a set of clinical diagnostic criteria to define anaphylaxis.[1] This definition has been widely adopted and played a key role in optimizing anaphylaxis recognition and management across healthcare settings.[2]

In the recent publication, "Persistent, refractory, and biphasic anaphylaxis: a multidisciplinary Delphi study", Dribin TE et al. described a set of consensus definitions on persistent, refractory and biphasic anaphylaxis, and also persistent and biphasic non-anaphylactic reactions, proposed by a panel of 19 experts in allergy/immunology and emergency medicine, conducted using the Delphi methodology. [3]

These definitions standardize the terminology used to describe anaphylaxis outcomes, ultimately facilitating communication between healthcare providers and patients and among research personnel. There were, however, uncertainty as to whether the definitions can be applied to ***infants*** because symptoms are usually more difficult to detect in this age group. In this definition, anaphylaxis that persists for 4 hours or more would be considered as "persistent"; and anaphylaxis that recurs within 1 to 48 hours would be considered as "biphasic". Authors acknowledged the difficulty in ***clear time delineation*** in view of the insufficient data. Change in the time period will affect the sensitivity of the definition as well as the prevalence of the conditions. The authors also clarified that this set of definitions were not intended to dictate management plan of anaphylaxis patients, including the period of observation or need for hospitalization, but rather patient care should be guided by individual patient and allergen presentation.

What was not discussed in this article was the importance in risk stratification of patients presenting with anaphylaxis. It has been reported that some factors, such as delayed in use of epinephrine, use of β-Blockers/ACEI, medication as a trigger, uncontrolled asthma and elevated tryptase or mast cell disorder, have been known to increase the risk for severe and potentially fatal anaphylaxis.[4] Since there is still no specific test that can reliably predict the outcome of allergen exposure in a sensitized individual, stratification based on patients' risk factors would be a good way to assist clinical decision-making and intervention strategies.

Allergen immunotherapy as a potential treatment but also a risk factor of anaphylaxis

Avoidance of allergen remains the mainstay of long-term treatment of anaphylaxis. However, accidental exposure to allergens as a cause of reactions are common with more than 50% of children having allergic reactions within 3 years of observation.[5] This is the reason why allergen immunotherapy has been of increasing research interest in the past decade. Allergen immunotherapy (AIT) is believed to be the closest thing to a "cure" for allergy. However, immunotherapy itself is a trigger of potentially severe anaphylaxis, hence recognition of the potential possible risk factors and implementation of appropriate measures to prevent and manage severe systemic allergic reactions are emphasised.[4] It is recommended that patients who have received AIT should be observed for at least 30 minutes in a supervised medical facility staffed with medical personnel trained to recognize and treat anaphylactic reactions, including timely administration of epinephrine.[6]

Education and empowerment is the cornerstone of anaphylaxis management

A comprehensive management of anaphylaxis patients between allergy specialists, emergency medicine, and primary care providers are necessary. Therefore, education dedicated for front-line physicians cannot be overemphasised. Allergists are advised to provide written emergency action plans to guide treatment of food-induced allergic reactions. On the other hand, patient education and empowerment are believed to be the best option to ensure effective long-term care. Patients and parents should be educated on how to properly read and interpret product ingredient labels and avoid cross-contamination with their known allergen during food preparation. They should be advised to carry a medical identification bracelet and inquire about allergen exposure at restaurants. Structured validated educational programs across the community, integrating health professionals, dietitians, psychologist, pharmacists, patient organization and the food industry (figure 1) is the most effective means to improve patient care and outcomes.[7]

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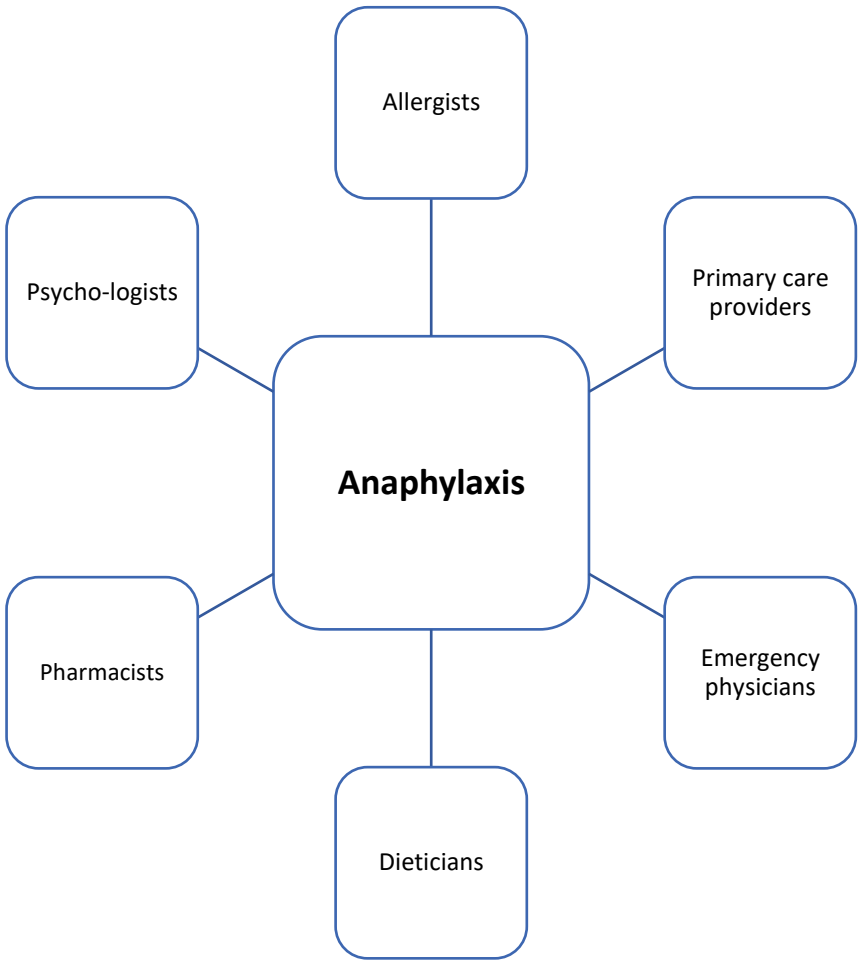
Figure 1. Integrated clinical care pathway developed by multidisciplinary and multi-professional teams.



Beta-lactam antibiotic allergy delabeling in children

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According to the American Academy of Allergy, Asthma & Immunology (AAAAI), hospitalized patients who report unverified penicillin allergy have longer lengths of stay and greater serious drug-resistant infections.[1] These patients are more likely to receive alternative antibiotics (eg, vancomycin, a quinolone or a carbapenem) that can be associated with higher costs and/or risks for adverse effects. More frequent use of alternative non-beta-lactam antibiotics also may lead to greater rates of resistant gram-positive (eg, *Enterococci* and *Staphylococcus*) and gram-negative (eg, *Klebsiella*) strains within the community. Treatment or isolation of patients affected by these resistant microbes is associated with increased costs, poorer patient outcomes, and other burdens.[1] For these reasons, in 2014, the Choosing Wisely program of the American Board of Internal Medicine Foundation recommended that clinicians not overuse non-beta-lactam antibiotics in patients without a comprehensive evaluation for any reported history of penicillin allergy. Additionally, President Obama released an Executive Order for a National Action Plan for combating antibiotic-resistant bacteria in 2015. This plan focused on aims to reduce the emergence and spread of resistant bacteria and infections, which included promoting antibiotic stewardship in hospital and ambulatory settings. In relation to the launch of this national antibiotic stewardship initiative, the AAAAI is advocating for more routine testing for patients with a history of allergy to beta-lactams. The performance of drug allergy testing will likely lead to reduced costs of care, enhanced patient safety, and improved outcomes of care.[1] In 2018, a study published in the journal Pediatrics reported that the potential annual cost savings of 67,000 emergency department visits by children was $192,223, but an astounding 80% of primary care physicians did not know that their patient had been cleared of the drug allergy from testing.[2] Based on these findings, the American Academy of Pediatrics issued a press release advocating for more to be done so that allergy test results are clearly communicated to parents and the entire health care team.

Sobrino and colleagues recently further investigated the costs of drug allergy testing in children.[3] This year long, prospective, observational study took place between 2017 to 2018 and included 40 children referred to their allergy service for suspected beta-lactam allergy. Three out of the 40 children were indeed confirmed to have the suspected beta-lactam allergy, but other tolerable beta-lactam antibiotics were found for them. The authors measured the total direct healthcare costs, which was $125.95 per patient, direct nonhealthcare costs, which was $22.55 per patient and indirect nonhealthcare costs, which reached $159.61 per patient (Table I). In total, these equated to $308.11 per patient. Presumably, the currency presented was in euro. These results were similar to two studies previously performed in adults.[4,5] Another study estimated the lifetime costs for patients labelled as allergic to penicillin before age 10 years old were $1,893 additional to those without such antibiotic allergy label.[6] Taken together, drug allergy testing for paediatric patients would equate to a total saving of $1,584.89 per patient.

One must bear in mind that the total savings would be fully applicable with the assumption that none of these patients will develop more beta-lactam antibiotic allergy over their entire lifetimes. More longitudinal research is needed to understand how future development of drug allergies would influence the cost of care, and this will be important for the healthy population as well as those with frequent, repetitive exposures to beta-lactams such as patients who are prone to reinfections. Repeated antibiotic exposures may increase the risk of developing a new antibiotic allergy in the future. Additionally, costs of maintaining healthcare facilities, testing equipment and kits, financial reimbursements for medical personnel, absence from work for parents vary between individual countries. The cost-saving impact of allergy testing must therefore be further studied in other health systems, such as within the context of our local area.

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Table I. Costs of allergy testing for beta-lactam antibiotics in 40 children in Spain.[2]

	Factors	Total Cost	Cost per patient
Direct Healthcare Costs	• diagnostic tests (skin tests, patch tests, challenge tests, total and specific IgE) • healthcare personnel • other materials and infrastructure (building maintenance expenses)	$5038.03	$125.95
Direct Nonhealthcare Costs	• number of visits • travel expenses per visit (estimated based on distance from home to clinic, with $0.21 per km)	$901.87	$22.55
Indirect Costs	• loss of working hours for legal guardians or • hourly minimum basic wages in Europe if parents unemployed	$6384.35	$159.61
Total Costs	Combined of above factors	$12 324.25	$308.11

Review on in vitro diagnostic options for type 1 food allergy

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Food allergy is gaining public awareness and it's an important cause of anaphylactic reactions. Proper workup and investigation are crucial to patient management. Hence, knowing the various options and limitations of diagnostics assays is essential for proper patient care.

Tryptase assay has been established for the workup of anaphylaxis. Tryptase is a mast cell mediator that is degranulated during mast cell activation. It is compared in pairs, with measurements of serum level taken during the acute allergic event versus the baseline level, for evidence of recent mast cell degranulation. The utility of tryptase in drug or venom allergy is more well established compared to food allergy. Nevertheless, recent studies also revealed its role in food allergy. Dua et al published a study on the diagnostic utility of tryptase in food allergy that investigated the tryptase levels in 160 peanut allergic adults upon peanut challenge. A rise was observed in 100 of 160 (62.5%) reactions and 0 of 45 placebo challenges, and they suggested a rise in tryptase of 30% was associated with food allergic reaction.[1]

The gold standard test for the diagnosis of food allergy is a double-blind, placebo-controlled food challenge (DBPCFC), in which increasing doses of food (or placebo) are administered under medical supervision. However, oral food challenges are time-consuming, costly and have a potential risk for anaphylaxis. In practice, the likelihood of an IgE-mediated food allergy is usually assessed first by checking sensitization through detection of allergen-specific IgE (sIgE) to the implicated food either in serum or through skin prick tests (SPTs). However, sensitization sometimes does not correlate with clinical reactivity. A positive blood or skin test result is not diagnostic on its own, and a false-positive rate of greater 50% has been reported in population-based studies.[2-4] This potentially leads to unnecessary dietary exclusions, social restrictions and anxiety that further impair nutrition and quality of life.

Due to the limitations of sIgE testing, some researchers have investigated the role of sIgE/total IgE or IgG_4/IgE ratios. However, there is no concrete evidence on their diagnostic values and therefore their use remains controversial. In the recent decade, component resolved diagnostics has revolutionized the workup in the field. Instead of testing the IgE level against the whole allergen extract, IgE responses against the allergen component molecules are measured. These new advances help to improve the assay analytical sensitivity and specificity, providing additional information on the cross reactivities and marker for the primary sensitization source. The assay can also be performed in a multiplex format, such as the immuno solid-phase allergen chip (ISAC), revealing a more thorough sensitization profile that may be helpful for complicated cases.

Apart from the sIgE assay, cell function assays also provide important information as part of a food allergy workup. In recent publications, especially for peanut allergy, basophil activation test has been shown to facilitate patients' risk stratification. Along with routine workup, basophil activation test helps to decrease the number of patients requiring food challenges.[5] Lately, some research groups have also investigated the utility of studying mast cell activation as part of a food allergy workup. Some employ specific cell lines while others have used primary human blood-derived mast cells (MCs) generated from peripheral blood precursors. The mast cells are then sensitized with patients' sera and incubated with the allergen. Subsequently, mast cell degranulation was assessed by flow cytometry and release of mediators. Preliminary data in a peanut allergy cohort is promising. In one publication, it even outperformed the skin prick, sIgE and basophil activation tests.[6] Nevertheless, the assay is technically demanding, especially in the aspect of mast cell culture. Further studies are required to explore its role in routine clinical setting and application in other food allergies. Overall, application of cell-based assays is limited by the need of fresh blood, and the methodology is technically demanding. Moreover, standardization of the assay across different laboratories is challenging and hence, less commonly available in routine clinical settings. Hence, some of these diagnostic tests are available at the Clinical Immunology Laboratory at Queen Mary Hospital, while others are under development (Table).

Conclusion

The field of food allergy diagnostics is rapidly evolving, and component resolved has now been incorporated into standard clinical practice. Various cell function assays, such as the basophil activation test and the most recently introduced mast cell activation test are technically challenging that limit their general application, although they are promising if they can be improved in the future.

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Table. Laboratory assays currently available in the Clinical Immunology Laboratory, Queen Mary Hospital.

Assays	Specimen requirements	Arrangement logistics**
Tryptase	5 mL clotted blood (red-top tube)	1st sample must be drawn within 4 hours of the onset of anaphylactic event 2nd sampling >24 hours after recovery from the anaphylactic event Store at 2-8 °C (not longer than 48 hours) if not able to send to lab within the day of collection
sIgE	5 mL clotted blood (red-top tube)	
Basophil Activation Test	Two 3 mL blood in EDTA (purple-top tube)	Fresh sample (within 2 hours) is required

**Consultation with the Clinical Immunology Laboratory for arrangement is required.

Topical treatments for mild-to-moderate atopic dermatitis: an update

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Atopic dermatitis (AD) is a chronic, pruritic, inflammatory skin disease that affects patients of all ages worldwide. The global prevalence of AD is approximately 15-20% in children and 1-3% in adults while the local prevalence of AD is estimated to be around 13.4% in Hong Kong.[1,2] More than half of the patients first experience symptoms of AD before 1 year of age, and many symptoms persist well into adulthood.[3] AD has a great impact on patients' quality of life including sleep disturbance, depression, and impaired psychosocial functioning—all of which cause psychological stress in the caregivers of paediatric patients.

Topical treatment for AD

The mainstay treatment for patients with AD is topical therapies, which are used not only by patients with milder disease severity, but also by patients with moderate-to-severe AD, in conjunction with systemic treatment.

Topical Glucocorticosteroids

After adequate use of moisturizers, topical glucocorticosteroids (TCS) are the first-line therapeutic agents for AD.[3] TCSs can be categorized into seven classes or low, medium, high potency and super-potent types (Table 1). These classes have been developed based on the vasoconstrictor assays and clinical efficacy. The best choice of TCS is often based on multiple factors, including the glucocorticosteroid molecules and vehicles, anatomical area and extent of skin involvement, patient's age, disease severity and the treatment response (Table 2). However, local and systemic side effects of TCS secondary to misuse and abuse have been well-recognised such as epidermal atrophy over the face and skin folds, perioral dermatitis and steroid-induced acne/rosacea.[4] As a result, regardless of the severity of AD, some patients and their carers express fear and anxiety about using TCS, leading to the 'steroid-phobia phenomenon' which affects medication adherence and long-term disease control.[5] According to one study, 38% of the caregivers were reluctant to use TCS, while no significant difference was noted in the carers' family history of AD, age or gender.[6,7]

Topical calcineurin inhibitors

Steroid-free topical treatment may help reduce overuse of TCSs and their associated side effects. Topical calcineurin inhibitors and TCSs had similar rates of improvement in dermatitis control (81% vs 71%; risk ratio (RR) 1.18 95% CI 1.04-1.34;p=.01)) and treatment success (72% vs 68%; RR 1.15 95%CI 1.0-1.21;p=.04)).[8] Calcineurin inhibitors were associated with higher costs and frequency of adverse events, including a higher rate of skin burning (30% vs 9%; RR 3.27, 95% CI 2.48-4.31 ;p<0.00001) and pruritus (12% vs 8%; RR 1.49; 95% CI 1.24-1.79 ;p<0.0001). There were no differences in the rate of skin atrophy, infections or serious adverse events requiring discontinuation of therapy. Corticosteroids, therefore, remain as the therapy of choice for atopic dermatitis (evidence 1a).[8]

Topical phosphodiesterase 4 inhibitor

Crisaborole ointment, 2%, is a non-steroidal topical treatment for mild-to-moderate AD.[9] Although its mechanism of action is not clear, phosphodiesterase 4 (PDE-4) inhibitor inhibiting the phosphodiesterase type 4 enzyme is known to suppress the secretion of pro-inflammatory cytokines, such as tumour necrosis factor (TNF) alpha.

As of January 2020, it was approved in the United States, Australia, Canada and Israel for use in patients aged ≥2 years. Its use has been further extended to infants aged 3 to <24 month with mild-to -moderate AD in a phase IV open-label study involving 137 infants.[9] About 30% of patients achieved clear or almost clear skin with more than 2 grade-improvement after 28 days of continuous treatment. Clinical improvement were observed at day 8, day 15 and continued through day 29 after the 28-day treatment period. About 6% patients reported application site pain or discomfort, while 3% experienced erythema.[9] No new safety issue was identified. Regarding the systemic exposure of crisaborole of infants aged 3 to <24 months, it was comparable to that observed in patients aged ≥2 years.[9-11]

Biologics and small molecules

Application of crisaborole ointment over sensitive skin areas such face, genitalia, and intertriginous areas has been associated with dermatitis, and other topical treatments can cause similar or worse side effects.[12] Therefore, biologics such as dupilumab and small molecular therapies such as Janus Kinase inhibitor (JAKI) are emerging therapies for moderate -to-severe AD in the current era of personalised medicine.[13] Topical application of tofacitinib (JAKI) ointment has undergone phase II clinical trial, which showed significantly greater efficacy versus placebo, with early onset of effect and comparable safety and local tolerability compared to control vehicle. JAK inhibition through topical delivery is potentially a promising therapeutic target for AD.[14, 15]

In summary, topical treatments for AD are the mainstay of management. Efficacy of steroidal and

non-steroidal topicals treatment are similar, while cost and potential side-effect would be factors guiding the choice of treatment for patients with AD.

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Table 1. Commonly used topical glucocorticosteroids and its potency ranking.

Super potent (class 1)	Clobetasol propionate 0.05% gel, ointment, cream, lotion, foam, spray, shampoo
High potency (class 2-3)	Betamethasone dipropionate 0.05% cream, gel and ointment Mometasone furoate ointment 0.1% ointment Triamcinolone acetonide ointment 0.1%/0,05% and cream 0.5%
Medium potency (class 4-5)	Betamethasone dipropionate lotion 0,05% Betamethasone valerate cream and lotion 0,1% Fluocinolone acetonide 0.025% cream, ointment
Low Potency (class 6-7)	Hydrocortisone cream 0.1%

Table 2 Factors affecting choice of Topical Glucocorticosteroid (TCs)			
TCs Potency	**Low**	**Medium**	**High**
Anatomical area of application	Face, eyelids, intertriginous area	Trunk and limbs	Palm, sole, scalp
Severity of skin lesions	Mild	Moderate	severe
Extent of Body surface area involvement	Large area*	Large area*	Small area
Treatment response after application	Poor clinical response→may switch to higher potency		Good clinical response→may switch to lower potency
Patient's age	Children: may start with low potency TCs	Adult: may start with medium potency TCs	
Suitability of vehicle	In general, glucocorticosteroid molecule in an ointment vehicle is more potent than the same molecule in a cream or lotion base. Gel or foam preparation tend to be readily absorbed and has a drying effect.		

*Caution for potential systemic absorption

A practical guide to prescribing intranasal preparations for allergic rhinitis

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Allergic rhinitis (AR), characterised by four cardinal symptoms, namely nasal itchiness, sneezing, rhinorrhea and nasal obstruction, is a common disease around the globe. The responses of this IgE-mediated allergic reaction are manifested in 2 phases, i.e. early phase and late phase. The early phase is triggered by mast cell degranulation and the resultant release of mediators including histamine, prostaglandins and leukotrienes, leading to the onset of acute nasal symptoms (i.e. nasal discharge and sneezing) within minutes following allergen exposure. The late phase response, occurring over a period of hours after allergen exposure, results from the chemotaxis of T lymphocytes, eosinophils and basophils to the nasal mucosa. The cellular recruitment and the continued release of cytokines from these cells induce and perpetuate the inflammatory response, which is associated with the persistence of acute symptoms and nasal obstruction as a result of nasal tissue remodeling.[1-3]

Not only can allergic rhinitis impair quality of life, but it can also contribute to other diseases such as asthma.[4,5] Therefore, prompt medical treatment and optimal symptom control are crucial. Apart from allergen avoidance, pharmacological agents available to treat AR include antihistamines, corticosteroids, decongestants and anti-leukotrienes, of which intranasal corticosteroids (INCS) have shown to be the most effective class of medication. INCS is highly effective at relieving sneezing, rhinorrhoea, nasal obstruction and ocular pruritis, redness and tearing.[4-6] Although the maximal effect is generally achieved after 2 weeks of administration, symptom improvement can be observed as soon as 3 hours after administration. Therefore, INCS is the drug of choice for cases when antihistamine alone fails to provide sufficient symptomatic control, moderate to severe symptoms, nasal polyposis or severe obstruction.[4-6]

In Hong Kong, intranasal preparations, particularly corticosteroids, are commonly prescribed to adult and paediatric patients with AR. Despite comparable clinical efficacy in symptomatic control, the licensed ages, indications and dosages vary amongst different INCS preparations. Therefore, physicians should be aware of the differences between each product to ensure safe and effective prescribing. Table 1 provides a summary on the different INCS preparations in the treatment of perennial allergic rhinitis (PAR) and seasonal allergic rhinitis (SAR) that are available in the market in Hong Kong, according to locally approved prescribing information. All of these are also available in the Hospital Authority formulary.

One of the products, Dymista®, is a combination product containing both INCS and intranasal antihistamine (INAH) (fluticasone propionate and azelastine). INAH is able to relieve nasal itchiness, sneezing and rhinorrhoea, but not nasal obstruction. Compared to oral antihistamine, INAH has a faster onset of action (within 15 minutes) and it is proven to be more effective in treating AR symptoms.[5,6] In a recent meta-analysis, INAH was found to be superior to oral antihistamine as add-on therapy to INCS in patients with AR.[7] In a focused guideline update by the AAAAI/ACAAI in 2017, the combination of INCS and INAH may be considered in patients aged 12 years or above with moderate to severe SAR.[8]

Despite adequate and appropriate medication prescribing in response to AR symptoms, poor technique on using intranasal devices compromises their efficacy and contribute to treatment failure.[4] Thus, device-specific training should be thoroughly delivered, particularly in patients prescribed with a new intranasal preparation. Patients should be educated on proper (1) priming and (2) technique of nasal spray application, which are further explained as follows:

(1) Priming

Prior to administration, the intranasal device should be adequately primed to ensure dosage uniformity. The number of actuations required for priming and the necessity of reprime vary amongst the different INCS products. In principle, for newly opened devices, after gentle shaking, the device should be primed by pumping a few sprays, usually 5 to 10 pumps, directed towards the air or until a fine mist is produced. Also, it is advisable for patients who are using INCS preparations intermittently to verify if a fine mist can be produced by actuating 1 pump to the air when the device has not been used for a certain period of time (2-7 days in most INCS preparations; 30 days for Avamys®). If not, the device should be reprimed.

(2) Stepwise Approach in Counselling on the Use of Nasal Sprays[4,20]

1. Gently blow the nose to clear excess mucus and particles
2. Tilt head slightly forward or maintain in a neutral upright position
3. Gently shake the bottle for at least 5 to 10 seconds
4. Place spray nozzle into the nostril, using right hand for left nostril and left hand for right nostril technique
5. Direct the nozzle to the side or laterally, but not the septum
6. Actuate the device while gently breathing in
7. Breath out through the mouth
8. Repeat Step 4-7 if needed

To conclude, intranasal corticosteroids and intranasal antihistamines are effective in relieving symptoms of allergic rhinitis when they are used with appropriate techniques. Therefore, when intranasal treatment fails to produce symptomatic control of AR, intranasal device techniques should be assessed and reinforced prior to dose titration or addition of medications. This article provides a summary and comparison of the different commercially available intranasal preparations in the Hong Kong market and a stepwise approach to educate patients on the use of intranasal sprays with the aim to assist improve prescribing effective use of medications.

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Table 1. Summary of the licensed ages, dosages and common adverse effects of intranasal corticosteroid preparations in the treatment of perennial and seasonal allergic rhinitis, registered for use in Hong Kong.

Drug	**Brand (Strength)**	**Licensed Age**[9-15]	**Licensed Dosage**[9-15]	**Adverse Effects**	**Remarks**	**Relative Cost**
Fluticasone furoate	Avamys® (27.5mcg/ spray)	2 years	*2-11 years:* Initially 27.5mcg (1 spray) per nostril once daily; may step up to 55mcg (2 sprays) per nostril once daily *≥ 12 years:* 55mcg (2 sprays) per nostril once daily	Epistaxis Headache Nasal & throat dryness Nasal & throat irritation	The novel nasal spray device delivers doses as a fine mist, with a comparatively smaller and more consistent droplet size (20-50 in diameter). The design facilitates an even dose distribution over a wide area, maximise drug retention in the nasal mucosa, and minimises throat irritation and unpleasant aftertaste.[16]	++++
Mometasone Furoate	Nasonex® (50mcg/ spray)	2 years	*2-11 years:* 50mcg (1 spray) per nostril once daily *≥12 years:* Initially 100mcg (2 sprays) per nostril twice daily; may step up to 200mcg (4 sprays) per nostril once daily	Headache Epistaxis Pharyngitis Nasal irritation	Other licensed indications: - Treatment of nasal polyps - Treatment of symptoms associated with acute rhinosinusitis in patients aged 12 or above without signs of symptoms of severe bacterial infection - Adjunctive treatment to antibiotics in the treatment of acute episodes of sinusitis (≥ 12 years)	++
Fluticasone Propionate	Flixonase Aq® (50mcg/ spray)	4 years	*4-11 years:* 50-100mcg (1-2sprays) per nostril once daily *≥12 years:* 100mcg (2 sprays) per nostril once daily - May step up to 100mcg (2 sprays) per nostril twice daily in severe rhinitis	Headache Unpleasant taste & smell Epistaxis		+

Drug	Brand (Strength)	Licensed Age[9-15]	Licensed Dosage[9-15]	Common Adverse Effects	Remarks	Relative Cost
Beclomethasone Dipropionate	Beconase® (50mcg/ spray)	6 years	Initial: 100mcg (2 sprays) per nostril twice daily - Consider dose reduction if symptoms controlled	Epistaxis Nasal & throat dryness Nasal & throat irritation Unpleasant taste & smell		+
Budesonide	Rhinocort Aqua® (32mcg/ spray, 64mcg/ spray)	6 years	*6-11 years (32mcg/spray):* Initially 32mcg (1 spray) per nostril once daily; may step up to a maximum 64mcg (2 sprays) per nostril BD (i.e. 256mcg/day) *≥ 12 years (64mcg/spray):* 128mcg (2 sprays) per nostril once daily OR 64mcg (1 spray) per nostril BD - Consider dose reduction if symptoms controlled	Local irritation Epistaxis Nasal secretion	Other licensed indications: - Preventive against nasal polyps after polypectomy - Symptomatic treatment in nasal polyposis	++
Ciclesonide	Omnaris® (50mcg/ spray)	SAR: 6 years; PAR: 12 years	100mcg (2 sprays) per nostril once daily	Headache Nasopharyngitis Epistaxis Sinusitis	The use of ciclesonide 50mcg-100mcg (1-2 sprays) per nostril once daily was shown to be safe and effective in treating patient aged 2-11 years with PAR[17,18]	+++
Azelastine & fluticasone propionate	Dymista® (137mcg and 50mcg/ spray)	12 years	1 spray per nostril BD	Epistaxis Headache Unpleasant taste & smell	Licensed age of Dymista® is 6 years in the US[19]	++++

Ask the Expert

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This section aims to provide up-to-date, evidence-based, yet easy-to-understand allergy information to our Nursing and Allied Health (NAH) members. In this issue, we have invited Dr. Alson Chan to provide some updates in Aeroallergen Allergy: Diagnosis and Treatment.

Aeroallergen allergy: diagnosis and treatment

Q: Is aeroallergen allergy common in Hong Kong? What are the most common aeroallergens seen in this area of the world?

A: Aeroallergen allergy is common in Hong Kong. Allergens in both outdoor and indoor spreading through the air are collectively called aeroallergens. The major aeroallergens in our locality are derived from dust mites, fungi, cats, dogs, cockroach and pollens.

Q: How is aeroallergen allergy diagnosed? How can you tell it apart from a common cold or flu?

A: Aeroallergen allergy is usually suspected after clinical assessment, then the diagnosis is confirmed by either skin prick tests or blood tests for specific IgE levels. Skin prick tests involve the use of a solution containing the suspected allergen placed on the patient's skin. A sterile lancet is then put on the skin to quickly prick through the surface layer of the skin via the solution. A small itchy red bump will soon appear at the site of skin pricking if there is sensitization to that particular allergen. Blood tests for specific IgE detect the amount of circulating IgE produced against the suspected allergens. With the use of ImmunoCAP or new microarray nanotechnology, we can now test for hundreds of suspected allergens and its components using only a small sample of blood.

As aeroallergens are found in our environment spreading through the air, our body parts in close contact with the environment will be affected. They can be stimulating our nose causing runny nose, itchy nose and sneezing; affecting our airways causing repeated coughs, shortness of breath and wheezing; contacting our eyes causing redness, itchy eyes and excessive tear; or attacking our skin causing skin redness, itchiness and rash.

Sometimes the initial symptoms and signs of aeroallergen allergy may be similar to the common cold or flu, but allergic diseases can usually be identified by their persistent and recurrent nature. A common cold or flu may last for about a week, but aeroallergen allergy will be recurrent and persistent for many months, or sometimes lifelong. There will not be any fever in aeroallergen allergy, and sometimes the triggering allergens such as cats, dogs, and dust mites can be easily identified to be associated with the specific symptoms and signs.

Q: Is aeroallergen allergy related to the climate?

Yes, many aeroallergens such as dust mites, fungi and pollens are more active and grow faster during summer season under higher temperature and humidity. Pollens are more abundant in spring and summer period. So global warming is causing a prolonged pollination period, and a prolonged period with higher dust mites and fungi density in many areas around the world, leading to more allergic diseases.[1] Besides, 'thunderstorm asthma' has been described in some areas after a severe thunderstorm or typhoon leading to a sudden surge of asthmatic attacks.[2]

Q: How is aeroallergen allergy treated?

The treatment strategies involve three aspects: (1) symptomatic treatment; (2) allergen avoidance and (3) allergen desensitization. Symptomatic treatment using topical or systemic medications (such as anti-histamines) is the commonest first line treatment strategy. It helps to achieve quick but transient relief from allergic symptoms even before identifying any causative allergens, but recurrence is common after the drug effect has passed. To achieve allergen avoidance, the best way is to identify the triggering allergen by appropriate diagnostic test(s) and then implement specific avoidance measures according to the doctor's advice. If the symptoms of allergic disease are still persistent or fluctuating after the above measures, an allergy specialist consultation is advisable and allergy workup should be carried out to confirm the exact triggering allergen(s) so that a corresponding allergen specific immunotherapy program can be designed with aims at long-term relief and recovery.

Q: When do you need to do allergen immunotherapy? What route is best (SLIT vs. SCIT)? Is there any contraindication?

Allergen specific immunotherapy can be applied to allergic diseases with known allergen triggers. The

threshold for applying this treatment usually depends on the severity of the allergic disease, the quality of life of the patients and the availability of the specific allergen extract for allergen immunotherapy. If an allergic disease remains persistent or recurrent, and disturbs the quality of life (e.g. affecting the concentration in school or at work, or disturbing the sleep quality), then one should consider allergen immunotherapy, which is the only available root cause treatment aiming at long-term, partial or complete curative control. It can be given via sublingual or subcutaneous routes. The more popular way of administering allergen immunotherapy is via the sublingual route (sublingual immunotherapy, or SLIT). As it avoids the need for repeated injections at the clinic, it is well received, especially by many children, adolescent and adults with busy lifestyles.

There are a few contraindications for allergen immunotherapy: active severe systemic autoimmune disorders that are not responsive to treatment; malignant neoplasia; uncontrolled or severe asthma; poor adherence to instructions, and (for sublingual immunotherapy) eosinophilic esophagitis. Other relative contraindications include beta-blockers usage, immunodeficiencies, severe psychiatric disorders and previous serious systemic reactions to allergen immunotherapy. High intensity physical exercise should also be avoided shortly before or after the administration of allergen immunotherapy.[3]

Q: How effective is allergen immunotherapy for aeroallergen allergy? What is the adverse reaction rate?

Allergen immunotherapy is a well-established treatment that can achieve long-term clinical benefits for allergic diseases. It is the only therapy that can change the natural history of allergic diseases, not only improve symptoms but also reduce the need for medications (such as anti-histamines and corticosteroids). It induces immune tolerance resulting in objective changes that are persistent for years after the cessation of treatment. A recent meta-analysis by the World Allergy Organization showed that allergen immunotherapy (both subcutaneous and sublingual) provided significant favorable treatment responses when compared to placebo in major randomized controlled clinical trials. A recent controlled clinical trial focused on sublingual immunotherapy for house dust mites in Hong Kong also revealed a favorable treatment response for local patients suffering from allergic rhinoconjunctivitis, asthma and atopic dermatitis.[5]

The most common adverse reactions for allergen immunotherapy are mild local reactions such as itchiness or erythema. The safety profile of allergen immunotherapy has been thoroughly evaluated in both the adult and paediatric populations. Both subcutaneous and sublingual allergen immunotherapy are considered safe and well tolerated when administered correctly under appropriate medical supervision.[6]

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Overseas Meetings

CHEST 2020 (The American College of Chest Physicians Annual Meeting 2020)
17 – 21 October 2020 / Chicago, USA (https://chestmeeting.chestnet.org/)

American College of Allergy Asthma and Immunology (ACAAI) Annual Scientific Meeting 2020
12 – 16 November 2020 / Phoenix, USA (https://annualmeeting.acaai.org/)

Local Meetings

Hong Kong Institute of Allergy Annual Scientific Meeting 2020 (HKIA 2020)
11 October 2020 (https://icc.eventsair.com/hkia-asm-2020/registration/Site/Register)

Autumn Respiratory Seminar of Hong Kong Thoracic Society and CHEST Delegation Hong Kong and Macau
7 November 2020 (https://hkts.hk/)

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