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Message from the Editors

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I hope everyone has enjoyed a safe and refreshing Easter break. I am honoured to take up the tenure of editor-in-chief. I am extremely grateful for the unfailing support from the council and my associates. My predecessor, Dr. Jaime Rosa and his team have left us a true legacy and garnered various attentions. Thus, the Newsletter has become a topical and succinct must-read for those that practice allergy on a daily basis.

At the time of writing, HK is preparing to initiate the relaxation of various social restrictions upon the receding fifth wave tormented by the Omicron variant. As a result, facilities such as cinemas and gyms will re-open. Face to face classes will resume. Work from home will cease, and in like manner; but HK will never be the same again.

The unprecedented 5th wave since the 31st of December 2021 has run its course and has accumulated 740000+ and 44000+ confirmed positive cases by nucleic acid test and rapid antigen test respectively; let alone umpteen undocumented, unreported and asymptomatic infections in the community. Sadly, the CHP of the DH has recorded over 9000 fatal COVID cases, arguably one of the highest case fatality rates among the Omicron hit regions and nations. The lion's share was ascribed to the abode of unvaccinated elderlies; situated in poorly managed residential old age homes. Conceivably, among the infected, there were some to "die with" COVID due to comorbidities instead of simply to "die of" COVID.

Nonetheless, recurrent news detailing healthy children succumbed to acute necrotising encephalitis, pictures of corpses loaded in emergency rooms and long queues stationed outside compulsory testing centres were among many of the pointers reinforcing the painful reality of the virus being far from a seasonal flu. A silver lining though is perhaps millions of people would have acquired immunity through either natural infection and/or from vaccination.

While we mourn for many tragic losses, we praise the bravery of health care professionals and essential workers who have risen to the challenges and held our fort during the dire crisis. Furthermore, no words can express our immense gratitude for the staunch support from our Mainland experts, health care compatriots and countless builders, all individually unsung heroes that kept our city afloat.

We feel proud of many of our institute's comrades who have been part of this saga, fighting fearlessly and engaging relentlessly in various "battlefronts" such as acute emergency services, intensive care units, community isolation facilities, and vaccination centres, et cetera.

We take pride of our Institute's academicians and clinicians who have stretched their productivity in churning out quality scientific papers, setting up guidelines, dishing out webinars and educational materials. Many have committed their valuable time and effort to public educations and media engagements.

Collectively we play a significant part in our leadership role of preaching for vaccine allergy safety while debunking myths and taboos.[1,2] As of now, HK has recorded a total of 15,590,730 jabs which accounts for over 92% and 86% eligible people who have had their first and second jabs respectively.[3] Our Institute has collaborated with patient support group HKAA on a recent survey amongst allergy people about their vaccination experiences which identified majority of allergic suffers have experienced safe vaccinations and only 5% of them required medical attention following vaccination. However, about a third of overall responders had expressed hesitancy to receive further shot.[4,5] So there is still much work to be done for us in supporting allergy community.

The Editor Team is extremely grateful to all the contributors of current Spring Issue at this extraordinary time. We thank for them for giving us priority among their various pressing commitments.

On food allergy clinical management and diagnosis, we have Dr. Gilbert T. CHUA and Prof. Edmond S. CHAN who depicts the principle and practice of food ladders for facilitating the development of natural tolerance for children with egg and milk allergy and its associated risk and benefit in accordance to allergy office practice. Dr. Agnes S.Y. LEUNG, Dr. Christine Y.Y. WAI, Prof. Ting Fan LEUNG and Mr. Kevin K. M. CHENG narrate the diagnostic approach to shellfish and highlight the pros and cons of old (Skin prick testing, Specific IgE, oral food challenges) and new (Component Resolved Diagnostics and Basophil activation test) diagnostics.

We are what we eat. Nutrition is part of the important preventive strategies. Dr. Alice S.S. HO shares her tips about antioxidant's importance in her article of Diet and Asthma. Dr. Sonal HATTANGDI-HARIDAS gives us much food for thought,

perhaps Hong Kong's urban malnutrition with high prevalence of Vitamin D deficiency that feeds up cytokine storms in COVID-19 patients. A resonate hypothesis that invites further investigational efforts to confirm or refute it. Ms. Sabrina W.S. MOK updates us on the current position of COVID-19, diet and nutrition with succinate take home messages like exact dosing of various vitamins and minerals.

On respiratory allergies, Dr. Terence C.C. TAM and Dr. Julie K.L. WANG give us an update on the current position of bronchial thermoplasty in managing difficult asthma amidst the era of availability of effective biologics. Dr Birgitta Y.H. WONG shares an insightful paper on the expression of SARS-CoV-2 receptor ACE2 in endotypes of chronic rhinosinusitis with nasal polyps (CRSwNP). It lends support to our usual advice to allergic patients that the use of intranasal glucocorticoid therapy should not be a risk factor for SARS-CoV-2 infection and such treatment should be continued during the infection.

Happy reading! Stay healthy! I hope we can see each other soon, face to face, with our facemasks off.

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Diet and asthma

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Many traditional nutritional factors and health patterns change due to the "Westernization" diet in many developed countries.[1] Few studies have investigated the association between diet and non-communicable diseases like asthma.

In an international study of asthma and allergy in childhood, over a million kids revealed a consistent inverse relationship between the prevalence rate of asthma, allergy and eczema with increased intake of plants, starch, grains, and vegetables.[2] If these findings could be generalized with the average daily intake of these foods increased, it is postulated that a significant reduction in symptoms prevalence may be achieved.[2] Researchers have proposed that people in developed countries are likely to have a diet with less fresh fruit and vegetables, resulting in an increased susceptibility to potentially harmful inhaled substances by reducing the antioxidants defences within the lungs.[3]

The respiratory tract lining fluid forms an interface between the respiratory tract and the external environment. It thus begins the first line of defence against oxidative damage, which plays a vital role in asthma.[4] Oxidative damage is pivotal in the pathophysiology of asthma. Antioxidants protect against oxidative stress.[5] These may be endogenous, including a range of antioxidant enzymes such as glutathione peroxidase and superoxide dismutase, or exogenous, such as vitamin C, vitamin E, carotenoids, and flavonoids, which are obtained from the diet, particularly from fruits and vegetables.[5] Edgar R. and colleagues quantify the level of the oxidative stress by measuring the oxidation products in the exhaled breath which drops with increasing consumption of fruits and vegetables.[6] There is a further drop with a combined consumption of more plants, fruits, vegetables and fewer animal foods.

Asthmatic subjects had a lower whole blood level of total carotenoids, lutein, β-cryptoxanthin, lycopene, α-carotene and β-carotene when compared to healthy subjects.[4] The accumulating evidence suggests that diet influences the response of the lung to inhaled allergens and irritants.[4] Thus, it is possible that the reduced carotenoid levels in asthma are a result of increased utilization in the presence of excess free radicals.[4]

Antioxidant-rich diets are associated with reduced asthma prevalence. However, direct evidence that altering the intake of antioxidant-rich foods affects asthma has been lacking. Wood et al. carried out a study to prove that changing the intake of antioxidant-rich foods affects asthma outcomes.[7] Forty-six asthmatic adults were randomly assigned to a high-antioxidant diet, i.e., five servings of vegetables and two servings of fruit daily and 91 asthmatic adults with low-antioxidant diet, i.e., less than two servings of vegetables and one serving of fruit daily 14 days. For the low- antioxidant diet group, forty per cent chance of relapse into asthma exacerbations within three months. If people take the high-antioxidant diet, they can cut the exacerbation rate in half, down to twenty per cent. Asthmatic subjects provided with a low antioxidant diet for two weeks led to a significant worsening of lung function and asthma control score. These findings are highly significant for patients with asthma. Suggesting that omitting antioxidant-rich foods from the diet for even a short period will have detrimental effects on asthma symptoms.[7]

A group of stable asthmatics were recruited to see if low antioxidant intake affected their asthma control in 10 days.[8] These subjects were then randomized cross-over supplementation trial to see if the effect would be reversed by dietary supplements with a lycopene-rich diet for seven days, with a ten-day wash-out period between each treatment. The lung function performance and asthma control score deteriorate in 10 days after low antioxidant diets. After treatment with a supplemental high antioxidant diet, there was a significant improvement in airway inflammation compared with placebo.[8] Interestingly, the low antioxidant diet consumed by patients during the initial phase of this study, which incorporated one serving of fruit and two serves of vegetables per day, is typical of western diets. Hence, this study indicates the potential for standard western dietary patterns to worsen lung function and asthma control. Cutting down fruit and vegetable intakes can impair lung function within just ten days but adding fruit and vegetables can help with asthma was the second phase of the study. In conclusion, asthmatic patients should be encouraged to increase fruit and vegetable consumption to reduce asthma symptoms and exacerbations.

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Food for asthmatics

Update on the current position of bronchial thermoplasty (BT)

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Burden of severe asthma

Asthma is the most prevalent chronic respiratory disease worldwide.[1] The 2019 National China Pulmonary Health (CPH) study put the prevalence at 4.2%.[2] The Web Database by Australasian Severe Asthma Network (ASAN) estimated that as many as 39.4% of asthma patients have uncontrolled symptoms and 3.4% would meet the European Respiratory Society / American Thoracic Society (ERS/ATS) definition of severe refractory asthma.[3] Patients with severe asthma experience higher rates of exacerbations, increased morbidity and disproportionate use of healthcare resources. Despite medications working in majority of severe patients, the implications for the subset of those who remain uncontrolled are significant.[4]

Safety & efficacy of bronchial thermoplasty (BT)

In addition to its contractile function, airway smooth muscle (ASM) is an important source of inflammatory cytokines and chemokines, and its alteration has been shown to be involved in multiple pathophysiological pathways in asthma.[5] Bronchial thermoplasty (BT) involved the use of controlled, therapeutic radiofrequency (RF) energy to reduce the amount of ASM, and was approved by the Food & Drug Administration (FDA) in 2010 for the treatment of severe asthma.[6] A complete course of BT treatment typically involves 3 sequential, minimally invasive bronchoscopic procedures scheduled 3 weeks apart. During each procedure, the patient is put under general anesthesia or deep sedation, and the RF catheter is introduced through the working channel of a flexible bronchoscope to deliver the ablation energy to airway of different lung segments under direct visualization. Each procedure typically lasts for 1.5 hours, and the patient can be discharged the next day if well.

The initial safety and efficacy data came from 3 small, randomized control trials, namely the Asthma Intervention Research (AIR), Research in Severe Asthma (RISA) and Asthma Intervention Research 2 (AIR2) trial published between 2006 – 2010.[7-9] Their results suggested that in severe uncontrolled asthma, BT was able to significantly improve Asthma Control Questionnaire (ACQ) & Asthma Quality of Life Questionnaire (AQLQ) score, reduce days-missed-from-work (by 66%), severe exacerbation (by 32%) and emergency department visits (by 84%) from 6 weeks post-treatment onwards to the end-of-study timepoint at 1 year.

The latest long-term efficacy data for BT was published in 2021. The follow-up study confirmed that the effect of severe exacerbation reduction at 10-year were sustained (Difference when compared to 1 year = 0.6% only), and quality-of-life measurements and spirometry were similar between year 1, year 5, and year 10. In terms of safety, there was a 7% increase in new radiological bronchiectasis in the treatment group, but all patients were asymptomatic.[10]

Patient selection in BT

BT is approved, and can be considered, for any adult patients with severe symptomatic asthma not controlled with high-dose inhaled corticosteroid & long-acting beta-agonist (ICS+LABA). However, as a direct consequence for manipulation of the hyper-reactive airways that is necessary before treatment completion and benefit kicks in, there is a transient but substantial risk of adverse event in the 6-week post-procedure period. As such, a lot of fine-tuning is required to select the most suitable candidate to undergo BT. In laymen's term, "*The asthma should be bad enough to require such invasive procedures, but stable enough (at certain time periods) to tolerate the 3 bronchoscopic procedures in order to reap the long-term benefits*". The multitude of general criteria and their narrow optimal window is illustrated in Figure 1.

BT in the era of biologics

With growing understanding on asthma phenotyping and the subsequent launch of multiple, highly effective biologics for severe asthma, re-evaluation of the place of BT within the treatment armamentarium is necessary. A simplified yet practical approach (summarize in Figure 2) that utilizes readily available parameters such as blood eosinophil and serum immunoglobulin E (IgE) level help stratify severe asthma into different endo/phenotypes with treatment implications. While omalizumab can be considered in severe atopic asthma (with raised IgE and

normal eosinophil), and mepolizumab (Anti-IL5), benralizumab (Anti-IL5R) & dupilumab (Anti-IL4/13) are good choices for non-atopic eosinophilic asthma (normal IgE with raised eosinophil), until tezepelumab (Anti-TSLP) becomes widely established and available BT fills the gap for the treatment of severe Th2-low asthma.[11]

It is important to note that rather than identification by certain hallmarks, the definition of Th2-low asthma is supported by the absence of the characteristic inflammatory and immune biomarkers of their Th2-high counterparts, and this group can account for as much as 50% of severe asthma.[12] Additionally, it is now known that up to 25% of severe eosinophilic and 32% of severe atopic asthma patients can be considered as non-responders to biologics, and BT may remain their only choice to gain back asthma control.[13,14]

Widening the scope of BT service

The bane of BT existence continues to lie in its precarious short-term risk-benefit ratio (i.e., sequelae of repeated manipulation of an unstable / hyperactive airway system vs. the proven long-term benefit in responders). To combat this, we need ways to (1) identify the "neediest" patient (in order to maximize the benefit that can be derived), (2) find ways to "condition" these "needy" patients to safely undergo the procedure(s), and (3) modify the BT procedure itself to minimize its intrinsic risks.

Multiple studies have confirmed that the following parameters help identify patients with the best response to BT – High baseline ACQ score, those with more than 2 exacerbations in the preceding 6 months, SABA use > 10/day, raised serum IgE level or eosinophil level at baseline, and those that received (any) treatment that enable normalization of their serum eosinophil before BT.[15-17] Knowing these factors used to be of academic interest only, but with the advent of biologics, patients with all endo/phenotype and instability can now be offered biologics (when appropriate) for a period to gain stability and may then be given a choice to switch to BT as a more finite treatment option.

The future - personalized BT

The most effective way to lessen the risk associated with BT is to reduce the number of procedure(s) necessary, and recent works have started on the concept of "patient-specific targeted bronchial thermoplasty". By using either (1) pre-procedure computer tomography (CT) and airway-structure reconstruction or (2) radioisotope ventilation imaging with ^{129}Xe / ^{3}He magnetic resonance imaging (MRI), preliminary studies have confirmed that regional lung ventilation quantification is a feasible method to select and plan regional treatment, thereby allowing patients to derive benefit from a single session of guided BT treatment that is comparable with three sessions of unguided treatment.[18,19]

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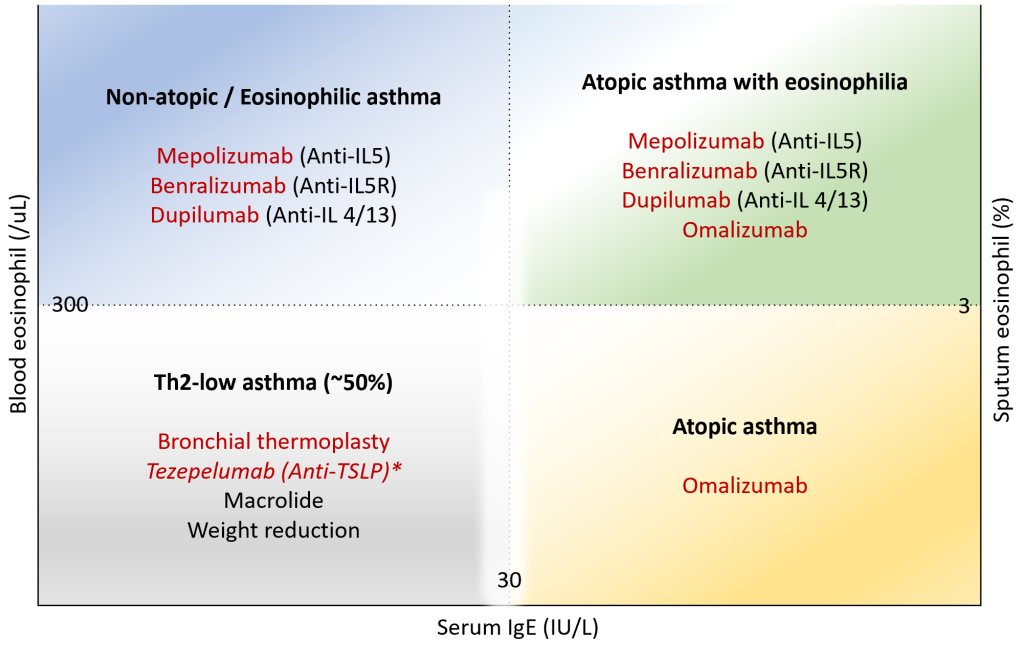
Figure 1. Graphic representation of the inclusion / exclusion criteria for BT procedure. Under the current indications, only those that fall within the green area are considered suitable candidate for BT.

		Too Severe / Uncontrolled	Suitable for BT	Too stable / Well controlled
Severity	GINA stage	**5 (High dose ICS + LABA)**		1-4 (Not severe enough)
	PBD FEV_1 (%)	< 65% (too severe)	**≥ 65%**	
	OCS (mg/day)	> 10 (too severe)	**≤ 10**	
Control	Symptom	**ACQ>1.5 / ACT<20**		Not enough symptom
	Daily SABA use	≥ 12 (too unstable)	**< 12 puff / day**	
Stability				
Past 2 years	ICU admission for asthma	Too high-risk	**No admission / intubation**	
Past 12 months	Admission for pneumonia	≥ 4 (Too unstable)	**< 4**	
	OCS bursts x asthma attack	≥ 4 (Too unstable)	**< 4**	
	Admission x resp. symptom	≥ 3 (Too unstable)	**< 3**	

GINA (Global initiative for Asthma), PBD-FEV1 (Pre-bronchodilator Forced expiratory volume in 1s), OCS (Oral corticosteroid), SABA (short-acting bronchodilator), AQLQ (Asthma Quality of Life Questionnaire), ACQ (Asthma Control Questionnaire), ACT (Asthma Control Test)

Figure 2. Decision chart based on the current knowledge of efficacy of add-on therapies in the most prevalent endo/phenotypes of severe asthma. Modified from Froidure A et al. Asthma phenotypes and IgE responses. Eur Respir J. 2016 Jan;47(1):304-19.



Expression of SARS-CoV-2 receptor ACE2 in endotypes of chronic rhinosinusitis with nasal polyps

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Chronic rhinosinusitis (CRS) is a common inflammatory disease of the nasal and sinus mucosa. It can be classified into CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP). CRSwNP can be further subdivided into eosinophilic (ECRSwNP) and noneosinophilic (nonECRSwNP) subtypes. ECRSwNP has a predominantly type 2 inflammation characterized by pronounced eosinophilia and high levels of IL4, IL5 and IL13 while nonECRSwNP is characterized by type 1 and/or type 3 inflammations.[1] SARS-CoV-2 employs angiotensin-converting enzyme 2 (ACE2) as the receptor for cell entry leading to infection and nasal epithelial cells show the highest expression of ACE2 among all investigated cell types in the respiratory system.[2] Thus the nasal mucosa is thought to be an important site for SARS-CoV-2 infection and replication.

Recently there is a paper published in 2021 by Wang et al summarizing the endotypes of chronic rhinosinusitis with nasal polyps and the potential impact of COVID-19 infection[3] by investigating the ACE2 expression in different subtypes. The author highlighted that factors leading to upregulation of ACE2 expression in host cells may be risk factors for SARS-CoV-2 infection. There are evidence showing that ACE2 is upregulated in hypertrophic cardiomyopathy, pregnancy, chronic obstructive pulmonary disease and smokers.[4-6] SARS-CoV-2 infection in patients with cardiovascular disease is relatively high, it is possible that the use of angiotensin receptor blockers upregulated the expression of ACE2. On the other hand, a cohort study showed that ACE2 expression was reduced in asthma, suggesting there might be protective factors against COVID-19.[3] As SARS-Co-V-2 likely binds to nasal epithelial cells prior to replicating, and chronic rhinosinusitis is a common condition, the author aimed to study the endotypes of CRSwNP in Chinese patients and their potential risks to SARS-CoV-2 infection in terms of ACE2 expression. The study was able to demonstrate that the expression of SARS-CoV-2 receptor ACE2 is significantly increased in nasal tissues of noneosinophilic chronic rhinosinusitis with nasal polyps (nonECRSwNP) patients which are predominantly type 1 and/or type 3 inflammation compared to eosinophilic ECRSwNP patients who are predominantly type 2 inflammation and control subjects. The upregulation of ACE2 expression in nasal tissues of nonECRSwNP with type 1 dominant inflammation might lead to an increased risk of SARS-CoV-2 infection.[3] However, the author commented that clinical association between CRSwNP and COVID-19 is still unclear. The method and findings were also clearly stated in another paper published by Wang et al in 2020 demonstating the expression of ACE2 by Western blot assay in nasal tissues of control subject, ECRwNP patients and nonECRSwNP patients.[1]

Wang et al further studied the regulation of ACE2 expression by oral glucocorticoids.[1] CRSwNP patients received a 2-week course of oral glucocorticoid. Nasal polyp tissues were collected before and after glucocorticoid treatment. The expression of ACE2 in the nasal polyp tissue was detected by RNA sequencing. The author found that glucocorticoid treatment on the expression of ACE2 was significantly decreased in nasal polyp tissues of nonECRSwNP patients but was not altered in nasal polyp tissues of ECRSwNP patients after 2 weeks of glucocorticoid treatment.[1] This might be due to the inhibition of type 1 inflammatory mediators such as IFN-γ. The author commented that the use of glucocorticoid therapy should not be a risk factor for SARS-CoV-2 infection in CRSwNP patients and should be continued during the infection.[1]

In conclusion, there remains limited data on the association of chronic rhinosinusitis and COVID infection. The upregulation of ACE2 expression in type 1 dominant inflammation of nonECRSwNP may have potential increasing risk of infection.

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The role of food ladders for egg and milk allergic patients

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Background

In May 2021, a girl in Ontario, Canada, who had milk allergy and long-standing asthma, passed away while undergoing a therapy which some have described as a milk ladder, although media reports suggest she did not increase beyond tiny amounts of muffin.[1,2] While the incident deeply saddens the allergy community, this article discusses the benefits, risks, and precautions of food ladders as a form of dietary advancement therapy, as well as ways to help our patients and families determine their best option through a shared decision-making process.

What is a food ladder?

A food ladder is a form of home-based dietary advancement therapy that gradually increases exposure to the allergenic food. The principle of the food ladder is to facilitate the development of natural tolerance through the gradual introduction of egg or milk containing food with increasing quantity and allergenicity through different cooking processes, typically from baked products (e.g., biscuits, muffin), to well-cooked forms (e.g., pancakes, waffles, hard-boiled eggs) and finally to less processed products (e.g., fresh mousse, fresh ice-cream).[3] Egg and milk ladders are the two typical forms of food ladders used clinically. It has been widely used in Europe and was initially designed to manage non-IgE-mediated food allergies.[4,5] Subsequently, application of the food ladder has been extrapolated to management of IgE-mediated milk and egg allergy, which has been generally safe and effective.

What are the benefits and risks of the food ladder?

Ball et al. retrospectively studied 86 children with mild milk allergies who started home-based milk introduction between 8 to 33 months of age. Fifty-four percent of the studied patients were able to freely consume stage 2 foods (e.g., waffles and scotch pancakes) and some stage 3 foods (e.g., cheese and heated butter), 9% all dairy except fresh milk/ice cream, and 18% were able to have a regular diet. None developed anaphylaxis or required epinephrine autoinjector.[6] Gotesdyner et al. studied 39 children under two years old with mild egg allergy and treated them using a structured graduated exposure protocol, and compared with a matched group of 80 children who were advised to strictly avoid egg at least until two years old or earlier natural resolution and followed to a median age of 69 months. The age of egg allergy resolution in the treatment group was significantly younger than the control group (median age 24 months vs. 78 months, $p<0.001$), and 82% of children in the treatment group were able to tolerate lightly cooked eggs, versus 54% in the control group ($p=0.001$).[7] Thomas et al. retrospectively reviewed 98 children with a median age of 40 months with mild egg allergy and were managed with egg ladder. 43% were able to complete the egg ladder over an average of 15.5 months. Only two had severe reactions, and one required epinephrine. The 2 with severe reactions resumed the ladder and progressed to the last two steps (lightly cooked whole egg or raw egg) successfully. A high proportion (78.7%) of the parents felt satisfied or very satisfied with the egg ladder.[8]

Patient selection for milk and egg-allergic patients

The primary benefits of home-based treatments such as milk and egg ladders are the demedicalized nature of them, and reduction in health care utilization (i.e. they allow practitioners the ability to allocate limited in-person appointments for oral food challenges and oral immunotherapy to other patients who are too high-risk for home-based treatments). Studies have shown that even home-based oral immunotherapy for IgE-mediated food allergy can be feasible and safe with very carefully selected patients,[9,10] which offers hope for facilitating early commencement of dietary advancement therapy where resources are limited with long waiting times, especially during the COVID-19 pandemic when there were limited non-emergency elective services and lack of regular in-office visits.[11,12] Emerging real-world evidence has demonstrated that performing oral immunotherapy for food allergy early, especially during infancy and preschool age, is significantly safer, more effective, and more likely to achieve sustained unresponsiveness than in older children.[13-17] It is also known that infants and toddlers have fewer allergic reactions involving the respiratory, cardiovascular, and neurological systems compared to older children.[18-20]

Nevertheless, like any other dietary advancement therapy, the food ladder is not risk-free. Most of the egg and milk ladder studies only included preschoolers with mild egg and milk allergies without a history of anaphylaxis, have no asthma or a well-controlled or no asthma, and families who could follow food allergy management and anaphylaxis action plans.[6-8] These selected preschoolers have a high likelihood of outgrowing their food allergy. In contrast, patients with a persistent food allergy phenotype such as those with previous anaphylactic reactions (especially when the respiratory and cardiovascular systems are involved), a prior history of allergic reaction at a very low trigger threshold, poor asthma control, and/or psychosocial factors (e.g. families unable to adhere to instructions or follow-up) are not suitable candidates for food ladders.[6,8] The food ladder should be administered by a well-trained and experienced healthcare professional with the necessary expertise and experience in food allergy and anaphylaxis management, performance of oral food challenges, and careful selection of patients for different dietary advancement therapies.[2] Patient informed consent should be obtained, and families should be aware of cofactors that could lower reaction threshold while on any dietary advancement therapy, including febrile illnesses, exercise, hot baths, dosing on an empty stomach, and an increase in total allergen exposure such as dust mite and pollen.[21,22]

A shared decision-making process to making the most suitable choice

Shared decision-making (SDM) refers to the process by which patients play an active role in managing their health. This is different from informed consent, in which patients only agree or disagree with a treatment option. SDM involves three steps: (i) creating choice awareness but providing an unbiased list of options, (ii) discussing options based on clinical relevance and current medical evidence, and (iii) discussing patient preferences, i.e., "what matters most" to the patient. It is essential to clarify goals and expectations of treatment, experience with previous management strategies, and possible fears. In the context of food allergy, it is important that the allergist provides different options to patients and families.[23] For example, if a patient has multiple food allergies, an option of milk or egg oral immunotherapy (OIT) instead of milk or egg ladders could be incorporated as part of a multiple food OIT protocol, which has also been shown to be safe and effective.[24] Alternatively, if the family is not ready to commit to any dietary advancement therapy, they can still opt for strict avoidance of food allergen while carrying an epinephrine autoinjector and be reassessed later for any spontaneous resolution of food allergy.[25] On the other hand, the allergist may decline or delay offering any form of dietary advancement therapy to with contraindications, e.g., poorly controlled asthma, language barrier for which an interpreter is not readily available, or behavioural problems for which daily dosing could be challenging.

Conclusion

Milk and egg ladders are safe and effective dietary advancement therapies, in patients who have a high likelihood of outgrowing their milk and egg allergies. Nevertheless, any form of dietary advancement therapy carries a risk of allergic reaction, including anaphylaxis, as these patients are still allergic to milk and egg at baseline. Careful attention needs to be paid to careful patient selection and the management of allergic comorbidities such as asthma, prior to initiating a milk or egg ladder.

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The diagnostic approach to shellfish allergy

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In the previous issue of Hong Kong Institute of Allergy e-newsletter, we have discussed about the epidemiology, clinical presentation, natural history and recent advances in the treatment of seafood allergy. In this current issue, we shall specifically focus on the current diagnostic approach to shellfish allergy.

Shellfish has been a primary ingredient in dishes of various cuisines. At the same time, it is an important food allergen particularly in coastal regions where consumption of seafood is high. The diversity of shellfish types, however, poses a challenge in the diagnosis of shellfish allergy. Conventional diagnostic approach to shellfish allergy is based on clinical history, different sensitization tests and oral food challenge (OFC), each with their advantages and limitations (Table 1).

Skin prick test

Skin prick test (SPT) is an *in vivo* diagnostic procedure which involves the introduction of small amount of allergen into the epidermis by pricking the skin surface with a lancet or needle. The introduced shellfish allergens will be in the form of either commercial ready-to-use extract preparation or in-house extract solution prepared with fresh or frozen shrimp (prick-to-prick [PTP]). Since epidermis is rich in mast cells, their contact with allergen via skin prick will trigger an immediate IgE-mediated immune response causing a wheal-shaped flare on the puncture site in 15 to 30 minutes. The sensitivity of SPT is generally reported to be high in Asia. In a Thai study, SPT to shrimp >3.5mm provided a sensitivity of 90%,[1] while a local study by our group reported a sensitivity of 93% using a cut-off of 3mm in identifying *Penaeus monodon* (tiger prawn)-allergic individuals.[2] Notably, in the *Litopenaeus vannaemei*-challenged Brazilian population, the sensitivity of SPT (*Penaeus setiferus*) was lower (71.4%).[3] The main issue with these commercial allergen extracts is that they contain different composition and concentration of proteins that vary between manufacturers.[4] Another problem is the cross-reactive response to tropomyosin in dust-mite and cockroach-sensitized individuals, which often lowers the specificity.[2,3] The diagnostic performance of PTP appears to be more heterogeneous. A study showed comparable diagnostic performance between PTP to fresh raw and boiled *Macrobrachium rosenbergii* and *P. monodon* and SPT using their extracts[5]. These SPT extract reagents showed good stability and remained sterile for up to a month. PTP test also appeared to be helpful in identifying patients with *M. rosenbergii* allergy, in which no corresponding commercial SPT extracts are available.[6] However, studies have shown that only SPT with crude shrimp extract, but not PTP with cooked shrimp extract, provided a superior discriminating value in identifying challenge-proven shrimp-allergic children.[7] It is very important to note that sensitization does not equate to clinical allergy, and false positive is common in atopic

dermatitis (AD) patients. In a recent study targeting Asian adults with AD, 46% of subjects without a history of seafood allergy developed positive reaction to at least one of the seven tested seafood allergens by SPT.[8] This will lead to an unnecessary avoidance of shrimp and/or other shellfishes in patients' diet and lower the intake of the important nutrients found in shrimp such as zinc, iron and magnesium. Other drawbacks of SPT include the risk of eliciting severe allergic reactions,[9,10] the requirement of skin unaffected by AD, need for patient cooperation during testing,[11] the potential interference by drugs[11] and the reported variability between users and devices.[12] However, SPT is still a clinically important tool to identify a patient's risk of allergies as it is highly sensitive, quick, easy to perform and relatively cheap compared to the other diagnostic tools.

Specific IgE test

Specific IgE (sIgE) test is an *in vitro* diagnostic test that measures the level of IgE antibodies against different individual allergens. When a person with allergy first encounters the food allergen, B cells in the body produces food-specific IgE antibodies which then bind to basophils and mast cells. This process is called sensitization. The subsequent consumption (exposure) of the same food allergen by the sensitized patient will lead to allergen-specific IgE antibodies crosslinking and trigger the release of chemical mediators such as histamine, prostaglandins and leukotrienes. The patient will then develop clinical allergic reactions such as hives, rashes, angioedema, bronchospasm or even anaphylaxis.[11] Therefore, measuring the amount of specific IgE antibodies in patient's blood sample may preliminarily reflect the severity of patient's allergic reaction to different shellfishes. Again, sIgE test measures patient's sensitization to shellfish as with SPT and does not directly reflect clinical allergy. A recent comparative study conducted in China, India and Russia showed that 4.7% 6-11-year-old children have a positive sIgE result of >0.7 kUA/L, but only 1.05% of them have both positive sIgE result and allergic symptoms after eating shellfishes in Hong Kong.[13] Measurement of sIgE to shrimp (raw *P. aztecus* and *P. setiferus*) tropomyosin yielded a higher specificity (92.8%) compared to sIgE to shrimp (75%) (f24 on ImmunoCAP: *Pandalus borealis, P. monodon, Metapenaeopsis barbata, Metapenaeus joyneri*) and SPT with crude shrimp extracts (*P. setiferus*) (64.2%) in the Brazilian population that are mostly allergic to *L. vannamei*, *P. brasiliensis* and *Xiphopenaeus kroyeri*. The sensitivity for all three methods was otherwise similar (71.4%). The specificity of sIgE to shrimp was generally lower in patients with dust mite allergy.[14] In a local study, sIgE to the tropomyosin of *P. monodon* using a cut-off of 0.35 kUA/L yielded a specificity of 80%, compared to the use of sIgE to shrimp (f24) which only provided a specificity of 35% in identifying *P. monodon*-allergic patients. All these findings suggested that use of component-resolved diagnostics (CRD), which aims at measuring sIgE antibodies to individual allergenic components in the form of proteins or peptides rather than the whole allergen extract, may overcome the shortcomings in SPT and sIgE tests. As with SPT, the level and diversity of allergens in the commercial extracts lacks standardization, as with the preparation methods with the use of raw or heat-treated extracts. Consequently, the accuracy varies among different commercially available platforms that provide sIgE testing, so as the cost and processing time. Generally speaking, the cost of sIgE tests to a panel of allergens is higher than that of SPT, and the processing time is usually 7-20 days.

Basophil Activation Test

Basophil Activation Test (BAT) is an *in vitro* state-of-the-art allergy diagnostic tool which detect immediate allergic reactions against suspected allergens using the technique of flow cytometry.[15] BAT requires patient's fresh EDTA blood. When the allergen is added to the blood sample, basophils are activated to upregulate the expression of CD63 and CD203 on their membrane surface. Using antibodies against CD63 and/or CD203 conjugated to fluorochromes, their expression on cell surface can be quantified using flow cytometry. BAT is commonly depicted as "food challenge in a test tube". Our group was the first to show that BAT yielded the highest Area-Under-Curve (0.88) for challenge-proven shrimp allergy when compared to sIgE assays and SPT. It achieved an optimal balance in sensitivity (87%) and specificity (94%), which can potentially reduce the number of OFC required for shellfish diagnosis. The main pitfalls of BAT are the lack of standardized laboratory procedures and data analyses, short sampling window as the test need to be completed within 24 hours after blood collection, long experimental duration up to 6 hours depending on the choice of kit, number of tested allergens and abundance of circulating basophil in the sample. Also, BAT requires a flow cytometer, which is a sophisticated instrument operated by training laboratory technicians and an expensive equipment not readily available in all laboratories. Overall, these attribute to the high cost of BAT among all the standard allergy tests. Accordingly, the optimal algorithm for diagnosing shrimp allergy at present will involve a stepwise approach with initial sIgE or SPT, which is followed by BAT on cases with inconclusive results to achieve a definitive diagnosis.

Double-blind, placebo-controlled oral food challenges

Currently, the gold standard for diagnosing food allergy is to conduct double-blind, placebo-controlled food challenges (DBPCFCs). The food allergen to be tested is added to a vehicle (foods that can mask the flavour of the food allergen and are not allergenic themselves), then patient is required to consume the food, from a small dose to incrementally larger doses at regular time interval.[16] For example, in our shrimp studies, shrimp meat was added to chicken meat, carrots and herbs to form patties. Patient is required to take 7-8 doses every 15-20 minutes, who will be observed for 2 hours after all doses have been taken to look for any allergic reaction. Before taking each dose, nurses have to conduct a thorough body check to see if patient develops any significant allergic reaction such as lip/eye/face swelling, hives and rashes. Patients will not proceed to the next dose if significant allergic reaction is observed or reported. Although DBPCFC is the gold standard of food allergy diagnosis, it is not routinely conducted in the clinical setting as it is labour-intensive and brings risks and inconvenience to patients. Firstly, dietitians need to prepare the tested food before the food challenge and nurses and doctors have to monitor the patients during the food challenge. Secondly, patients need to come

back to the hospital on at least 2 days (one day for placebo and another day for allergen-containing food), and they are at risk of developing severe allergic reaction such as anaphylaxis. Hence, the current research trend is to develop a reliable laboratory test that can accurately diagnose food allergy and predict the patient's clinical phenotype, thus reducing the number of food challenge required. The manpower and DBPCFC preparation cost in addition to the cost of patients' productivity loss will be far greater than the cost of BAT.

In conclusion, we have summarized different methods in the diagnosis of shrimp allergy, each with their pros and cons. The major obstacle to an accurate shellfish allergy diagnosis is the different sensitization pattern in shellfish-allergic patients and the cross-reactivity to mites. CRD, in place of extract-based SPT and sIgE tests, appears to be a useful screening tool and an accurate test in the diagnosis of shellfish allergy in mite-prevalent regions such as Asia, while BAT is an emerging and promising tool in selected patients where history and other diagnostic assays are not definitive for the diagnosis of shellfish allergy.

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Table 1. Comparison of different diagnostic tools in shellfish allergy

	Commercially available platforms	Whole extract/ allergen components	Species/components used	Advantages	Disadvantages
Skin Prick Test	- ALK-Abelló	Whole extract	- *Crangon penaeus*	- High sensitivity - Low cost - Results ready in 15 minutes	- Composition and concentration of SPT extracts vary between manufacturers - Low specificity due to cross reactive response with mite - Risk of eliciting severe allergic reaction - Requires intact skin and patient's cooperation - Potential interference by drugs such as antihistamines
	- Greer	Whole extract	- *Litopaenaeus setiferus/Farfantepanaeus aztecus/Farfantepenaeus dourarum*		
Specific IgE Test	- ImmunoCAP	Whole extract and allergen components	- *Penaeus monodon/Metapenaeopsis barbata/Metapenaeus joyneri)* - Tropomyosin from *Penaeus aztecus* (rPen a 1)	- High sensitivity - Able to screen multiple food allergies with small amount of blood sample in multiplex assay like ISAC	- Higher cost than SPT - Lack of standardization between different commercial extracts - Low specificity due to cross reactive response with mite - Relatively longer processing time (7-20 days) - Requirement of larger amount of blood samples for single-plex assay like ImmunoCAP if multiple food allergens are to be tested
	- FABER	Whole extract and allergen components	- *Litopenaeus vannamei* - Tropomyosin from *Litopenaeus vannamei* (Lit v 1)		
	- ISAC	Allergen components	- Tropomyosin, Arginine kinase and Sarcoplasmic Ca-bonding protein from *Penaeus monodon* (nPen m 1, nPen m 2 and nPen m 4)		
Basophil Activation Test	Nil	Whole extract and allergen components	- *Penaeus monodon* - Tropomyosin, Arginine kinase, Sarcoplasmic Ca-bonding protein, Troponin C, Triosephosphate Isomerase, Fatty acid binding protein from *Penaeus monodon* (rPen m1, rPen m 2, rPen m 4, rPen m 6, rPen m 8 and rPen m 13)	- Highest diagnostic accuracy (AUC) compared to SPT and sIgE tests - Optimal balance between sensitivity and specificity	- Higher cost than SPT and sIgE test - Short sampling window - Long process time up to 6 hours - Lack of standardization of laboratory procedures and data analysis
Double-blinded Oral Food Challenge	Nil	Nil	Nil	- Gold standard in diagnosing food allergy	- Highest cost, including staffs cost and cost of patient's productivity - Labor intensive, requires food preparation by dietitians and nurses to stand by during the challenge

Is urban malnutrition feeding cytokine storms in COVID-19 patients? Vitamin D insufficiency, a Hong Kong perspective

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The 5th Wave of SARS COVID-19, predominantly the Omicron variant, hit Hong Kong hard with unprecedented hospital admissions and mortality in the vulnerable. By mid-March 2022, 1,900 children were admitted with 2 yrs. and younger, being the highest proportion in PICU. Sudden complications, some fatal were reported with fainting, coma and convulsions. Over 6555 elderlies have succumbed.

Clinical presentations of COVID-19 include symptoms of viral infection and the life-threatening auto-immune response to the invasion. Termed 'Cytokine storm', this uninhibited release of inflammatory factors by the patient's immune system is comparable with a raging forest-fire destroying without precision. The T-cells becoming overactive have been implicated in excessive inflammatory cytokine release.[9]

What role does malnutrition play in facilitating immune overreaction? In Hong Kong, a developed city, which undernutrition could be undermining the health of a population?

Vitamin D (VitD) facilitates innate and adaptive immunity. It has potential links to regulation of cytokine storms, coagulopathies, cardiac and nervous system morbidity.[4] Its presence in the body at normal levels (30ng/ml or 75nmol/L) supports the healthy maturation of the immune system. VitD enhances cellular immunity in young children, importantly the regulation and differentiation of T cells.[13] Healthy levels of VitD are known to support protection from viral infection and bronchial inflammation especially in children.[14] (Table 2)

A 2018 study had shown 22-60% of HK infants had severe VitD deficiency below 25 nmol/L (10ng/ml).[5] Recent data published by HKU for the HK paediatric population found evidence of a progressive decline in serum 25(OH)D levels since social distancing measures first began in 2020 COVID-19 pandemic. By Nov 2021, VitD Levels were found to be declining at the rate of 6.32nmol/L per month and this is from an already lower baseline. Pregnant and breast-feeding mothers would also have a lower VitD levels due to reduced sun exposure unless supplemented.[17] Seventy-two percent of Hong Kong young adults were VitD deficient in 2017.[17] Vitamin D receptor polymorphisms which may cause dysfunction and VitD deficiency have been reported at a higher incidence in Chinese ethnicity including in Hong Kong.[10, 12]

This unrecognized population wide Low VitD status may add to grave complications in acute infections such as COVID-19. Studies have shown that lower Serum VitD levels in COVID-19 patients are associated with higher pro-inflammatory cytokine levels, increased viral presence, a higher risk of hospitalization, ICU admission and death.[3] VitD deficient patients (<20 ng/mL) have a 14 time higher risk of critical disease compared to patients with healthy VitD levels (≥40 ng/mL)(p=<0.001).[8] (Table 1)

Complications in lower VitD groups included dyspnea, 3-fold higher risk of arterial pO2<60mmHg and higher CRP.[1] Multi-organ systemic inflammation with encephalitis were documented in VitD insufficient and deficient paediatric populations from Turkey and UK. The UK study specifically looked at ethnic minority including Asians and also documented higher incidence of VitD deficiency in the infected children vs un-infected.[3, 7]

Urgent supplementation policy in vulnerable groups

Having present-day data of local deficiency, evidence from global studies and proof of healthy VitD levels in immune modulation, swift action is warranted to improve this easily modifiable factor in the war against COVID-19. The youngest age group and others, not eligible for COVID-19 vaccines are left further immunocompromised if VitD deficient. (Table 3)

Presently there is no known program of Vitamin D supplementation for the Hong Kong adult, elderly or paediatric population. As social distancing measures continue, urgent targeted therapeutic supplementation is needed to support immune regulation. Improvement of the VitD status of the Hong Kong population will be a cost-effective, ethical measure to support reduction of severe illness and hospitalizations during the COVID-19 pandemic and future viral illnesses.

A daily oral dose of VitD3 (Cholecalciferol) at 1000 IU (25µg) raises serum 25(OH)D levels by 15-25nmol/L over weeks/months without toxicity and is well within the range of safety.[19,20] In critical care, a larger loading dose is required, while daily moderate doses are efficient to improve respiratory outcomes in vulnerable groups.[19]

For supplementation, infants would need further categorization as formula-fed or breast-fed with the latter at a higher-risk of lower VitD status. Cholecalciferol food fortification at a population level

would prevent recurrence of deficiency and potentially reduce viral complication load on the over stretched hospital system during the pandemic and annual flu season.

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Table 1: VitD levels in relation to severe/critical COVID-19, moderate COVID-19 and healthy controls

Population studied	Severe/Critical COVID-19	Moderate manifestation COVID-19	Healthy controls	p value
N= 1176 Galilee Medical Center (GMC) in Israel.[8]	87.4%<20 ng/mL	34.3%<20 ng/mL		$p < 0.001$
N= 149 Bagcilar Training and Research Hospital, Istanbul, Turkey.[11]	10.1 ± 6.2 ng/mL	26.3 ± 8.4 ng/mL		$p < 0.001$
n=75 Paediatric Kirikkale University Hospital Turkey.[2]	not tested	21.5 ± 10.0 ng/mL	28.0 ± 11.0 ng/mL	$p < 0.001$

Table 2: Effect of serum 25(OH) D on immune modulation

1. Induces differentiation of T-regulatory Cells and inhibits Th17 cell proliferation by upregulate PLC-γ1 expression.[18]
2. Promotes secretion of anti-inflammatory cytokine TGF-β121.[18]
3. Suppresses pro-inflammatory cytokines such as interleukin-17 (IL-17).[18]
4. Vitamin D signaling is essential in regulating pro-inflammatory signaling of Th1 (a Th1 skew is noted in Broncho-alveolar lavage fluid $CD4^+$ T cells of COVID-19 patients as seen in VitD deficiency)[6]

Table 3: High-Risk population for VitD deficiency: conditions and medications known for lowering VitD levels.[19]

Conditions	Medications
Kidney, Liver Heart failure esp. Transplant patients	Glucocorticoids
Inflammatory and bowel malabsorption disease	Antiretroviral medication
Granuloma- forming disease such as Sarcoidosis, tuberculosis	Antifungals
Hypo-Hyperparathyroidism	Anti-Seizure medication
Hospitalized and ICU patients	Rifampicin
Obese	Cholestyramine
Elderly	
Oncology patients	
Pregnant, Breast feeding	
COPD, Asthma, Cystic Fibrosis	

COVID-19, diet and nutrition

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While the pandemic of COVID-19 persisted in 2022, the variant of Omicron has swept all over Hong Kong, bringing a huge burden to the local healthcare system. While vaccination is of uttermost importance, this article also reviews whether the quality of diet and particular nutrients may help prevent or treat COVID-19.

Micronutrient Supplementation

Vitamin C

Vitamin C is a water soluble vitamin with anti-inflammatory and antioxidant properties and patients often wonder if vitamin C supplementation can help prevent COVID-19 and reduce the symptoms once infected. According to the National Institute of Health (NIH) COVID-19 Treatment guideline, studies showed limited evidence of vitamin C in treating non-critically ill or critically ill COVID-19 patients.[1] A systematic review with 572 subjects, with dose of vitamin C (wither IV or oral) of 50 mg/kg day to 24 g/day also showed no significant difference in mortality, length of ICU stay, length of hospital stay and incidence of mechanical ventilation.[2] Another meta-analysis on micronutrient supplementations analysed four RCTS and five retrospective cohort studies with low risk of bias also showed that vitamin C supplementation (orally 1 or 8 gram daily; IV 50 mg/kg/day, 2-4 gram and 6 gram per day) did not have with reducing mortality, length of stay or intubation rate in cases with COVID-19.[3]

Recommendations: The use of vitamin C in treating patients with COVID-19 is inconclusive.

The Recommended Nutrient Intake (RNI) of 100 mg vitamin C per day is sufficient to maintain ordinary plasma levels in healthy adults above 18 years old and there are no additional benefits with vitamin C intake of 500 mg per day or above. The recommendation is encouraging at least two serves of fruits and three serves of vegetables daily, especially fruits high in vitamin C, e.g. strawberries, kiwi fruit, orange, mandarin, guava, bell peppers, etc. Food allergy patients should consume adequate fruits and vegetables from non-allergic sources and considering supplementation only when vitamin C intake cannot be met with whole foods.

Vitamin D

Vitamin D is a fat soluble vitamin that helps regulate calcium and phosphate in the body, produced by the skin mainly after exposure to ultraviolet radiation from the sun. It can also be consumed from dietary sources, such as fish, red meat, egg yolks, liver etc. The RNI for vitamin D is 10 mcg (400 IU) /day for adults and 15 mcg (600 IU) / day for elderly. Vitamin D deficiency can be quite common in developed countries, especially for patients with eczema.

A systematic review and meta-analysis showed that the serum vitamin D levels in patients with SARS-CoV-2 infection were significantly lower than the patients with negative results.[4] Another systematic review and meta-analysis showed although vitamin D did not reduce mortality of COVID-19 patients, it may be associated with shorter length of hospital stay and lower intubation rate, especially if taken immediately after getting COVID-19.[3] A systematic review comprised of 11 studies (six cohort studies, one case-control study and four cross-sectional studies), on the other hand, showed that vitamin D reduced the risk of COVID-19 infection, severity and mortality with a moderate level of confidence.[5] However, the causative agents and plausible mechanism of how vitamin D might have a protective effect are unknown.

Recommendations: Increased intake of food rich in vitamin D and getting adequate vitamin D from sun exposure safely are recommended for people at risk of COVID-19 infection. Vitamin D supplements may be given to patients with COVID-19 with vitamin D deficiency and might be considered for the primary prevention of COVID-19 infection and the management of patients with COVID-19. However, further intervention studies are needed to confirm the benefits.

Zinc

Zinc is a mineral and the RNI is 7.5 mg/d for female adults and 12.5 mg/d for male adults.

Dietary sources include seafood, meat, seeds and nuts, lobster/crab, wholegrains/legumes etc. and refined cereals lack Zinc. The amount formulated in multivitamin supplements normally ranges from 5 mg to 15 mg per serving. According to the 2014 total diet study in Hong Kong, most HK general adult population has adequate Zinc intake.[6] Population at risk of Zinc deficiency include elderly, people with CVD, diabetes, chronic respiratory disease etc.

Low levels of serum Zinc has increased susceptibility to infection and inflammation.

In a systematic review and meta-analysis, fives studies with 738 patients were revised and showed the Zinc supplementation is not associated with reduced mortality in COVID-19 patients.[3]

Recommendations: According to the National Institute of Health (NIH) COVID-19 treatment guideline, Zinc

supplementation against dietary allowance is not recommended for preventing COVID-19.[7] There is also insufficient evidence for the use of Zinc in treating COVID-19. The upper limit for Zinc intake is 40 mg /day for adults and an overdose can cause copper deficiency and Zinc toxicity.

Diet quality

While there were many studies focusing on micronutrient supplementation, the quality of diet is also important. A high quality diet is characterized by having more wholegrains (e.g. oat, brown/red rice, quinoa etc.), high in fruit, vegetables and nuts intakes while less in animal protein and fat, and processed/refined foods. A research with over 30000 COVID-19 patients in the US and UK showed that a dietary pattern with higher intake of plant-based foods (also regarded as having a higher diet quality) was associated with lower risk and severity of COVID-19.[8] Results from food consumption surveys with 27 food items were combined into 14 food groups. Each food group was then ranked with a score of one to five (five being of highest diet quality) and less healthy food groups were ranked in reverse scores. All food group scores were summed to obtain a total score of the Healthy plant-based diet index (hPDI), ranging from nine (lowest diet quality) to 70 (highest).

Another indicator, the diet quality index (DQS), was developed to quantity diet quality in accordance with the UK dietary guideline, consisting of five food components and a score of one to three (1: unhealthiest, 3: healthiest) will be rated depending on the consumption frequency. Scores from each food components were added up to a total score of five (lowest diet quality) to 15 (highest diet quality).

Results showed that participants in the highest category of the hPDI has significantly lower risk of developing COVID-19 than the lowest category of the hPDI, even after accounting for other healthy behaviors, social determinants of health, virus transmission measures. The inversion association was consistent using the DQS score and even more evident in areas of higher socio-economic deprivation.

Recommendations: Although purchase of fresh fruits and vegetables are easily perishable and may be hard to purchase/consume during quarantine or recovery, consider buying those with a longer shelf life, e.g. apples, oranges, mandarin, (even better if stored in the refrigerator), and canned corn, canned or dried beans and lentils etc. are also good plant-based choices to recommend patients as tolerated.

Long COVID and its association with Mass Cell Activation Syndrome (MCAS)

Long COVID is referred to ongoing signs and symptoms of COVID-19 up to 12 weeks and the most common symptoms include cognitive impairment or “brain fog”, GI symptoms, skin rashes etc. Research showed similarities of COVID-19 with Mast Cell Activation Syndrome (MCAS), whereby a wide range of symptoms were triggered in response of the release of mast cell mediators.[9] No studies have been done whether a low histamine diet may help alleviate the long COVID symptoms.

Recommendations: The Allergy UK and the British Dietetic Association suggest that more research is required whether a low histamine diet should be recommended in managing long COVID.[10,11]

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Overseas Meetings

EAACI 2022 (European Academy of Allergy and Clinical Immunology 2022)
1 - 3 July 2022 / Prague, Czech Republic (https://www.eaaci.org/eaaci-congresses/eaaci-2022)

ERS 2022 (European Respiratory Society (ERS) International Congress 2022)
4 - 6 September 2022 / Barcelona, Spain (https://www.ersnet.org/congress-and-events/congress/)

APAAACI 2022 PSAAI@50
1 - 4 October 2022 / Manila, Philippines (https://www.apaaaci.org/2022)

CHEST 2022 (The American College of Chest Physicians Annual Meeting 2022)
16 - 19 October 2022 / Nashville, Tennessee, USA (https://chestmeeting.chestnet.org/)

ACAAI 2022 (American College of Allergy Asthma and Immunology Annual Scientific Meeting 2022)
10 - 14 November 2022 / Louisville, Kentucky, USA (https://annualmeeting.acaai.org/2022/)