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Message from the Editors

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We've had a busy and thrilling time of summer and it gives me great pleasure to now welcome you to our Autumn Edition of Newsletter.

Hong Kong is coming back, but it's not yet better than ever when the US declared the pandemic 'over', the WHO was quick point out that isn't yet the case. In the same way, signs that Hong Kong is ready to open to the world with several back-to-back international events don't mean there isn't still work to do to improve residents' well-being. Whilst for us within the Institute seems much more work to be done for the increasing prevalence of allergy diseases.

HKIA is coming back, and has just staged her first post-pandemic physical our Annual Scientific Meeting on 25 September 2022 (Sun) at HKEC, though the audience was not as big as pre-pandemic but the quality, levels of science and intellectual exchange of the event were as superb as ever. The picture album in this edition captures the enthusiastic participants.

Unfortunately, Tak isn't coming back; we are deeply saddened by the passing of Dr. LEE Tak-hong (AKA, Tak by the Allergy Professional Community), Past President (2014-17) of our Institute and a world-renowned leader in the fields of asthma and allergy, on the morning of 26 August 2022. He literally was seeing patients and communicating with many of us on the very last day of his earthly life. Utter shocking! Three obituaries written by Past Presidents, Drs. Christopher Lai, Robert Tseng, Marco Ho and Current President Prof. Gary Wong are adapted in this Edition together with some rare and memorable pictures. Tak will be deeply missed and fondly remembered. His visionary leadership, passion and dedication to the development of the Institute and Hong Kong Allergy as a whole will always be cherished. His legacy will live on for generations to come.

Picture 1. Tak's Allergy Clinic Office. Lights out.

Perpetuating Tak's vision of recapitulating the "hub and spoke' allergy service model, Dr Philip LI Specialist in Immunology and Allergy & Chief of Rheumatology and Clinical Immunology, Department of Medicine, The University of Hong Kong, co-write a synopsis with his research associate Mr Andy K.C. KAN on Hong Kong's Drug Allergy Delabelling Initiative (HK-DADI) in Hospital Authority where hundreds of thousands carry penicillin allergy. HK-DADI is becoming a new Hub-and-Spoke Model in HA by reinventing a nurse-triaged evaluation protocol in penicillin allergy delabelling which could minimise the need of unnecessary skin testing in low-risk patients.

The CUHK team led by Dr. Agnes S.Y. LEUNG together with her dieticians: Ms. Chloris H.W. LEUNG, Ms. Ann W.S. AU, Allergen and Ms. Nicole P.F. LI, gives a comprehensive review on food allergen labelling with comparisons of local and global situations. Consumption of pre-packaged foods put allergic individuals at increased odds of severe allergic reactions compared to consumption of fresh or home-cooked foods underpins the need for improved allergen labelling practices in Hong Kong.

ENT surgeon with strong interest for children Dr. Birgitta Y.H. WONG offers a short report on the latest insight of allergic rhinitis in children with otitis media with effusion Nutritionist Dr. Sonal HATTANGDI-HARIDAS gives us some recent evidence on the relationship between Immunological disorders and vitamin D status on the pivotal role of an optimal Vit D Status in maintaining an optimal balanced immune response. She calls for more for local clinical research and clinical practices of timely identification of Vitamin D insufficiency.

Thank you to all of you that came to say hello to us in person and that shared your ideas on Newsletter. Please keep them coming and stay well.

With my best wishes to you all,

Dr. Marco H.K. Ho
Editor, HKIA e-newsletter
The Hong Kong Institute of Allergy

Picture 2. Dr Jane Chan (Founding Editor) hosted a dinner to Office Bearers, Editors and Associate Editors of Newsletter back in 2017.

In Memoriam of Dr. Tak LEE

Dear HKIA Members and Associate Members,

We are deeply saddened to share with you the passing of Dr. LEE Tak-hong, Past President (2014-17) of our Institute and a world-renowned leader in the fields of asthma and allergy, on the morning of 26 August 2022.

Dr. Lee will always be remembered for his unparalleled commitment to the development of Allergy in Hong Kong and his leadership and his long-lasting impactful services to the Institute. Most of us fondly called him Tak.

Tak retired from his Professorial post at King's College London and as Director of the Medical Research Council - Asthma UK Centre in 2011. He returned to Hong Kong and commissioned a new Allergy Centre at HK Sanatorium and Hospital (HKSH) in 2012. Since then, he has devoted himself to HK allergy and unified a distinguished team of colleagues to transform the professional credibility and public perception of the specialty. He convened the Hong Kong Allergy Alliance and documented the unmet need for allergists in HK in a published authoritative document. He is an exemplary role model and has inspired and mentored many allergy trainees and colleagues about career development. During his tenure of HKIA Presidency 2014-2017, he led the council, rewrote the constitution and transformed HKIA into an academic society with a professional secretariat; offered a new scheme to support pump priming grants for research and travel scholarships; promulgated HKIA practice guidelines, created an active subcommittee structure; and launched an informative newsletter, webpage and Twitter social platforms. He actively engaged colleagues from the universities, HA and the private sector in a cohesive partnership for the benefits of HK's community. Tak attracted substantial sums of uncommitted funding to HKIA. He emphasized the need for rigorous governance and had written detailed formal operational procedures for HKIA to avoid conflicts of interest. Tak fostered a sense of collaboration and community. He was an advisor and had promoted greater formal links between the Institute and patient support and charity - HK Allergy Association - to encourage public engagement and outreach. Tak's sustained dedication and contributions to leadership of the allergy community in HK and his transformative influence in the spheres of education, research, clinical service and outreach deserved the highest recognition of the President's Medal of the Institute in 2021.

Tak's visionary leadership, passion and dedication to the development of the Institute and Hong Kong Allergy as a whole will always be cherished. His legacy will live on for generations to come. He will be deeply missed and fondly remembered.

Dr. Marco HO
Immediate Past-President
Hong Kong Institute of Allergy

Prof. Gary WONG
President
Hong Kong Institute of Allergy

Obituary of Dr. Tak-hong Lee by Dr. Christopher Lai

Obituary by Christopher LAI, DM, FRCP, FHKAM(Medicine), FHKCP, Honorary Clinical Professor, Department of Medicine & Therapeutics, The Chinese University of Hong Kong

I will remember Tak as the ultimate fighter. While many would throw in the towel when facing seemingly insurmountable obstacles, Tak would plot meticulously with a cool head and fight with every fibre to achieve his goals. Tak's perseverance has served to advance Allergy as a medical and scientific specialty in Hong Kong, the UK and worldwide.

I witnessed the fighter in Tak when he asked me to advise on the respiratory side of his newly diagnosed systemic sclerosis several weeks ago. Despite the multitude and complexity of his various health issues, he already had formulated a clear and detailed plan on what would be required for this battle, after all, he had overcome serious illness from cancer three decades earlier whilst establishing himself as one of the pioneering leaders in his specialty in the UK and subsequently in Hong Kong. Emblematic of his meticulous nature and his thoughtful leadership, he had efficiently assembled a team of relevant specialists to advise him on his complicated medical conditions, and led each of us to work harmoniously towards the same goal.

I have known Tak since my days in the UK almost 4 decades ago. I was privileged to see him lecture at scientific meetings at that time, where he showed an impressive way of generating and effectively communicating innovative ideas. As a Hong Konger and world-renowned medical leader, he was greatly admired by us and regularly invited to speak at our respiratory and allergy meetings, even before he returned here in 2011.

One would be forgiven to assume after he retired from the UK at the pinnacle of his profession, he would put his feet up and simply enjoy the vibrant life in Hong Kong, especially in view of his long term health issues (which amazingly seemed not to impede his energy, enthusiasm and productivity). Not Tak, though, as his ongoing dedication to develop his beloved medical specialty, selfless desire to better colleagues and serve patients has led to long-lasting benefits for patients and communities in Hong Kong and worldwide. Tak's legacy within the medical profession in Hong Kong is an inspiration to myself and many others, which was motivated entirely for the betterment of others rather than for personal gain.

One of Tak's top missions was to establish Allergy as a specialty in Hong Kong, as he and his able contemporaries had in the UK. People here may not know that he actually started off as a respiratory physician but because of his strong research interest in asthma, he later became an allergist in the UK. Because of his then-existing specialist registration in Respiratory Medicine, achieving his goal of developing Allergy as a deservedly respectable specialty in Hong Kong presented some bureaucratic challenges. He first would need to additionally obtain a specialist title in Allergy, to enable him the platform from which to train young doctors within the specialty. It is a testament to Tak's professionalism and resilience that despite being one of the world's most prominent allergists that he dutifully took on the challenges of this task, securing the title of Specialist in Allergy after more than a year of cutting through red tape. This remarkable foresight from Tak subsequently allowed him to become the most influential leader in Allergy in Hong Kong.

Tak's next move was to gather people interested in the discipline to work together, inspite of the multitude of diverging opinions on how best to approach developing a largely overlooked specialty. To identify the 'right' people, Tak invited each of us, one at a time, usually at a bar over a glass (or quite often more) of beer – his favourite drink – to explore our views and

how we could contribute. The beer might have been a catalyst to bring out candid views or at least, it made the meeting more enjoyable in case there were some conflicting ideas. Through this exercise, he built a team that could work smoothly together toward the same goal. The rest is history, and he miraculously transformed the Hong Kong Institute of Allergy into an academically-oriented organization that not only held regular educational courses and meetings, but also encouraged research by funding worthwhile scientific projects in allergy. He also mentored Hong Kong's first ever locally trained allergist in adult medicine who is currently our only full-time academic staff in this disciple.

Tak knew it would take a lot more than his impressive achievements over the last 10 years to truly and firmly establish Allergy as a recognized specialty here. He knew he would need the support from the government to establish funded posts for trained specialists in Hong Kong, who in turn could contribute to the care of hundreds-of-thousand patients with disruptive and potentially life-threatening allergies. Through his leadership, an Allergy Alliance has been formed with health professionals of related specialties and lay persons who are stake holders in Allergy. Remarkably, Tak was able to convene a meeting for the Alliance just a couple of days before his death, promptly distributing minutes on the following day outlining various planned activities that would further his noble ambitions.

Tak was more than a hard-working professional. He enjoyed his golf and I was fortunate enough to share his joy at all the courses here. His ability to strategise and innovate shots were particular strengths in his game, in keeping with his ambition and problem solving ability he would exhibit professionally, although like many of us, his shot execution on the course might not always match his brilliant ideas. That did not worry Tak a bit. Unlike those who would moan after a bad shot, this gentleman would smile and could always see the funny side of the game.

I will always remember Tak as a noble person and a great leader who would never give up and fight gallantly for the right cause. When I asked him how his long-term disabling health issues had impacted him, he smiled and calmly said they actually made him a better person. No grudges, just forever so positive and graceful for whatever life threw at him, that's your Tak. Although he is no longer with us, his spirit and the 'Tak's way of problem-solving' will always be in our thoughts. May he rest in peace.

Obituary of Dr. Tak-hong Lee by Dr. Robert Tseng

Obituary by Robert TSENG, MBChB (Manchester) 1976, FRCP (Edin) (London), FHKAM (Paediatrics), BSc (St. Andrews), DCH (London), MRCP (UK)

In Nov 1989 I'd first met Tak on a slow train from Hong Kong to Guangzhou, China, to attend the first ever World Chinese Chest disease meeting. In those days there was no direct flights from London to Guangzhou. Tak was one of the two international Chinese scholar attending. International relationship had a hiccup after the June 4th incident, many invited Chinese overseas scholar had opted not to attend. In spite of his busy schedule as a newly appointed head of the department at a London hospital; Tak had prioritised his time to attend, as he felt the need of supporting motherland and the best way to show support would be a presence. He was the last to arrive and left as soon as he gave his talk. A typical pattern we are now all too familiar with. A true patriot who loves Hong Kong, a clansman who leads by his actions rather than words. He was late landing in Hong Kong and I stayed behind in order to accompany him. A little jetlagged, he chatted excitedly about his work on Eskimos, fish oil, food asparin and more, what a treat! I'd became a fan, an admirer of his academic endeavours and achievement ever since.

Fast forward to 2012, the Hong Kong Institute of allergy was excited to learn of the arrival of this academic giant and his intention to create a training programme as well subspecialty of allergy and immunology. To do so, he set up a clinic and various working groups in order to lobbying government. His initial enthusiasm was met with skepticism/inertia amongst some. To facilitate his wish, my contribution was to abdicate presidency of HKIA so Tak could take the helm. With his vast experience, hard work, charm, flare, the HK institute of allergy soon expanded vastly, training post was established. Confident in his cause and goals, Tak is not insensitive towards others. In the earlier years he'd often ask if he had, upset some. Last decade has seen allergy departments from the two Hong Kong's Universities working closely. Tak Lee's efforts in achieving this harmony is, for me, one of the legacies he leaves.

I shall miss you Tak. I am sore because your departure is so sudden, four days after our zoom meeting and two days after your email summary of the minutes in which you'd outline the future. Moreover, you have developed a culture locally of working in harmony, not discord.

At a personal level, it was good to learn that your life is coming together, reunited with your big, expanding clan, and finding yourself at peace at the one and only, with I presume the One and Only.

For me, you have only moved next door and we shall meet in the not too distant future. Meanwhile, your name will no doubt be oft uttered in our meetings, over coffee, or at the bar over a Gin and something.

Rest in peace, my friend. Condolences to the Lee Kee Clan.

Allergic rhinitis in children with otitis media with effusion

Dr. Birgitta Y.H. WONG

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Otitis media with effusion (OME) is the collection of fluid within the middle ear space due to inflammatory processes but without any features of acute inflammation. OME is prevalent among children with an estimated incidence of 20%. It is also the most common cause of hearing loss in children. Most of them are self-limiting but nearly 5% of children still require surgery.[1]

The pathogenesis of OME can be multifactorial including Eustachian tube dysfunction, infection of tubotympanum and allergy. However, the association between allergic rhinitis and OME has been controversial with many contradictory results and studies.[2] A study by Fernadez and McGovern on 113 children with OME, 92% were found to have allergy with positive skin prick test.[3] There was a recent paper published in 2020 by Norhafizah, Salina and Goh in a large paediatric ENT centre in Malaysia looking at the prevalence of allergic rhinitis in children with otitis media with effusion, common allergens and the hearing threshold in allergic rhinitis group versus the non-allergic rhinitis group.[2] A hundred and thirty OME children were recruited in this study. Skin prick test for aeroallergens and food allergens were performed. Hearing assessment with play audiometry or pure tone audiogram were used to identify the hearing threshold Tympanogram was done with type B tympanogram considered as otitis media with effusion and type C indicating a significant negative pressure and eustachian tube dysfunction. Rigid nasoendoscopy or flexible laryngoscopy was done to assess for adenoid hypertrophy. The patients were re-examined after 3 months.

For the result, the mean age of presentation of OME children in their study was 8.79 years old, ranging from 4 years old to 18 years old. 53% were 4-8 years old. The prevalence of allergic rhinitis in the OME children was found to be 52.3%. The three most common allergens in their group were DP, DF and Blomia. For food allergy, 40% were allergic to prawn, 33.8% to squid, 16.9% to fish and 15.4 to chicken meat. According to the ARIA guidelines, 13.2% of the children had intermittent mild allergic rhinitis, 25% had intermittent moderate-severe allergic rhinitis, 29.4% had persistent mild allergic rhinitis and 33.8% had persistent moderate-severe allergic rhinitis. On reassessment after 3 months from diagnosis, 54.6% had persistent OME. Up to 80.3% of the persistent OME children had allergic rhinitis. This demonstrated that allergic rhinitis is a statistically significant risk factor for persistent OME ($p<0.0001$).[2] The study also looked into other risks factors for persistent OME. Interestingly, based on the history, they found that 96% of the children with persistent OME had more than 4 family members in the household. Tonsillitis was not a significant risk factor. Exposure to cigarette smokes or passive smoker showed no significant association and the duration of breastfeeding was also not statistically significant. In their study, the author had excluded OME children with grade 4 adenoids as it is a confounding factor in developing persistent OME being a reservoir of bacteria.[2]

The study had a detailed analysis of hearing threshold across the frequencies with pure tone audiogram. They found that 500Hz was the most vulnerable frequency that is the low frequency hearing was more affected than the high frequency among the children. Besides, they clearly demonstrated that children with OME and allergic rhinitis had a significantly higher hearing loss compared to non-allergic rhinitis children.[2]

In conclusion, their study showed a significant difference in the prevalence of OME between allergic rhinitis and non-allergic rhinitis children.[2] Proposed mechanism is that allergy can lead to increased inflammation of the Eustachian tube and middle ear mucosa causing persistent negative middle ear pressure.[4] Rosenfield published a 28% spontaneous resolution of OME by 3 months and a 42% resolution by 6 months.[5] Goh et al in this study had a higher percentage of resolution of 45.4% in which they postulated to be due to the use of intranasal corticosteroid and oral antihistamine in the OME children with allergic rhinitis. Moreover, the parents were counseled on the compliance of the medications. The author proposed to optimize treatment to avoid unnecessary surgery in this group of children.[2]

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Allergen labelling— patients' friend or foe?

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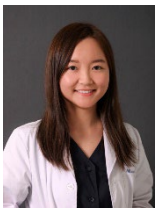

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To minimize unfavourable adverse food reactions in food-allergic individuals, strict avoidance of known allergens is often encouraged. Consequently, one of the cornerstones of safe food practices is food label reading for persons who have food allergies and caregivers who are responsible for them. Accidental allergic reactions to pre-packaged foods are nevertheless common, despite healthcare professionals' best attempts to teach their food-allergic patients to carefully read food labels. In a prospective observational study conducted by our team, pre-packaged meals were found to be responsible for 28% of adverse food reaction episodes. Consumption of pre-packaged foods put allergic individuals at increased odds of severe allergic reactions (anaphylaxis) compared to consumption of fresh or home-cooked foods.[1] This underpins the need for improved allergen labelling practices in Hong Kong.

Mandatory allergen labelling

1. Different types of allergens regulated between countries

Different food allergen labelling laws are being introduced and enacted by food manufacturers from different countries (Table 1).[2] Whilst it is mandatory for food manufacturers to clearly identify ingredients of major food allergens on pre-packaged foods, different countries have specific views of what foods constitute as major allergens. Comparison of allergens to be displayed on food labels is shown in Table 2.[2]

2. Inconsistent food allergen label presentation

Studies on food allergen labelling are being conducted in an attempt to identify ways to improve the labelling system to make it clear for food allergic consumers and their caretakers, which was also known as "Good allergen labelling practices", e.g., having the ingredients list contains simple food allergen name adjacent to the jargon name such as lactose (milk).[3] To date, no studies on food allergen labelling practices have been conducted in Hong Kong.

The Australia New Zealand Food Standards Codes updated their document last year with revised regulations on "good labelling practices".[4] The aim is to facilitate people who are looking up allergen information on pre-packaged foods for informed and safe food choices. For example, name of allergens displayed in the package must be in simple English, bold font, with adequate font size used for the mandatory declaration of food allergens. In addition, a separate allergen summary statement must also be printed on the same field of view and directly next to the ingredient list.

A study evaluating food allergen labelling practice in Hong Kong collected allergen labelling information from the entire catalogue of infant pre-packaged food (n=302) sold in a major local supermarket retailer.[5] Data showed that 16% of allergen-containing infant food products failed to use plain language for allergen declaration, whilst only 38% products used bold fonts or symbols to highlight the presence of allergens. Only 60% of the products included a separate statement to summarise the list of allergens; among which, 21% failed to place the

statement at immediate proximity to the ingredients list. The study also found that a majority of allergen statements (72%) are available only in English, while the rest were bilingual (25.2%) and in Chinese only (1.7%).5 Overall, the current allergen labelling practices in Hong Kong appeared unstandardised. There is an unmet need to regulate imported pre-packaged foods to provide clear and consistent labelling in order to improve allergen management and safety for food-allergic patients.

Precautionary allergen labelling

In addition to compulsory declaration of "common allergens" on food labels, precautionary allergen labelling (PAL) are statements to guide consumers on the potential risk of contamination of one or more food allergens during production and handling, in the format of such as "may contain traces of X", or "produced in a factory where X is also handled". This is voluntary in Hong Kong, and all aforementioned countries, however some countries like Japan prohibit the use of PALs6 (Table 1).

1. Inconsistent types of statement used

A market research on infant food allergen labelling conducted in Hong Kong found that around 20% of locally available pre-packaged infant products included PAL statements.[5] The rate is comparatively lower than that reported by other international studies which included mainly adult pre-packaged foods (56-69%). The most common format was "may contain traces of x" (44.4%), followed by "made in the same factory that handles x" (31.7%) and "made on the same equipment line that processes x" (7.9%). The research also suggested a variation in use of PAL possibly attributable to differences in allergen labelling practices of the import countries.[5] This is especially noteworthy when international imports of pre-packaged foods accounts for the majority of the total supply in Hong Kong.[7]

A study conducted by Holleman, et al. in the Netherlands indicated that food-allergic consumers (n=99, mean age=33.9 years) perceived PALs as "difficult to interpret" (>60%).[8] They also perceived different degrees of allergen contamination risk with the lowest being 'Produced in a Factory' to 'May contain' or 'Traces of' PALs ($p<0.001$), and 'May contain' was preferred over the other PALs, where in fact, all these statements should be taken as equal risk.

2. Misuse of PAL

Even though PAL is not intended to replace allergen risk analysis and management, most food products with PAL do not have detectable levels of the allergen(s) of interest. Therefore, they do not impose a risk for the vast majority of food allergic individuals.[9] The excessive use of PALs indeed exacerbates food allergic individuals and/or parents/caregivers of risk-taking to consume foods with PALs due to the limited food choices and additional economic burden, thus debatable among healthcare professionals about advising patients on whether it is safe to consume foods with PAL in allergen-restricted diets.

In 2018, an Australian study conducted by Zurzolo, et al. showed that 6.7% (n= 58/864) of respondents with known allergies self-reported anaphylaxis to packaged foods in which the allergen was not listed as an ingredient.[10] Among the 58 anaphylaxis cases, 53% of the suspected food triggers were not listed in the PAL statements, and 8.6% of the foods had no PAL statement.

3. PAL that reflects actual health risk

Few countries have set threshold for PALs. Switzerland allows PAL only if an allergen is present at a concentration above 1,000 ppm. Voluntary Incidental Trace Allergen Labelling (VITAL) is a scientific risk assessment developed for food manufacturers to assess the impact of cross-contamination and provide appropriate food allergen labeling in Australia and New Zealand.[11] VITAL 3.0 allergen labelling is determined by action levels, based on calculating the amount of allergenic protein likely to be in the maximum amount of a food eaten on a typical eating occasion (the reference amount). This is then compared with VITAL 3.0 reference doses for each allergen. Reference doses are based on the eliciting dose 01 (ED01), the amount of an allergen below which only the most sensitive 1% of the allergic population is predicted to react. PALs are assigned only if the product is likely to contain more than the reference dose. The science underpinning VITAL 3.0 is considered robust and peer-reviewed by researchers as the evidence for 14 allergens is based on EDs of oral food challenge studies that are continually added to the database. Other countries like Germany[12] and Belgium[13] have started to adopt the concept of action level in precautionary allergen labelling.

A PAL that reflects actual health risk may be more meaningful than using a threshold of a fixed concentration for all foods. However, the reference doses vary between countries, regions and populations and may need to be recalculated to achieve the agreed level of safety and it may raise burden on relabeling of imported goods.

The inconsistency in food labelling regulations and unregulated PAL use between countries not only make it challenging for food manufacturers to comply with the local market and international exports, it also confuses consumers when trying to make a purchase.

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Table 1. Food labelling laws of different countries

Country	Governing body	Food labelling law	PAL
United States	US Food and Drug Administration	Food Allergen Labelling and Consumer Protection Act	Voluntary
Canada	Canadian Food Inspection Agency	Food and Drugs Act and the Safe Foods for Canadians Regulations	Voluntary
Europe	European Commission	Regulation (EU) No 1169/2011	Voluntary
Australasia	Food Standards Australia and New Zealand	Australia New Zealand Food Standards Code, Legislation Act 2003	Voluntary
Japan[6]	Japanese Consumer Affairs Agency	Food Sanitation Act of the Ministry of Health, Labour and Welfare	Prohibit
Hong Kong[14]	Centre for Food Safety	Food and Drugs (Composition and Labelling) (Amendment) Regulation 2004	Voluntary

Table 2. Mandatory labelled allergens of different countries

Food	US	EU	Canada	Australasia	Japan	HK
Buckwheat					✓	
Celery		✓				
Crustacean	✓	✓	✓		Shrimp & crab	✓
Egg	✓	✓	✓	✓	✓	✓
Fish	✓	✓	✓	✓		✓
Cereal containing gluten		✓	✓	✓		✓
Lupin		✓		✓		
Milk	✓	✓	✓	✓	✓	✓
Mollusk		✓	✓			
Mustard		✓	✓			
Peanut	✓	✓	✓	✓	✓	✓
Sesame		✓	✓	✓		
Soybean	✓	✓	✓	✓		✓

Perpetuating Prof Tak Lee's vision with Hong Kong's Drug Allergy Delabelling Initiative (HK-DADI)

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Introduction

Professor Tak-hong Lee was one of the foremost pioneers of allergy in Hong Kong, guiding and leading his established Hong Kong Allergy Alliance even till the last days before his passing in August 2022. His spirit and dedication continue to live on with the Hong Kong Drug Allergy Delabelling Initiative (HK-DADI) being just one example of many transformative initiatives thriving from the foundations laid by Professor Lee during his remarkable career.

The Hong Kong Allergy Alliance was a group of individuals with an interest in allergy drawn from all specialties, professions and societies in Hong Kong. With just two practising Specialists in Immunology & Allergy at the time of writing, Professor Lee united the Hong Kong Allergy Alliance and published 'Allergy in Hong Kong: an unmet need in service provision and training' in 2015 (Figure 1)[1]. It was then the term 'Hub-and-Spoke' model was first coined and recommended as 'the best model for allergy service delivery' in Hong Kong. The 'hub' would act as a central point of expertise with outreach clinical services, education, and training provided to professionals in primary and secondary care (the 'spokes'). In this way, knowledge regarding the diagnosis and management of allergic conditions could be disseminated throughout the region.

Building the 'Hub-and-Spoke' model for drug and penicillin 'allergies'

Suspected drug and penicillin 'allergies' are very common in Hong Kong with a prevalence of 7% and 2%, respectively[2]. However, most penicillin allergy labels are found to be inaccurate and the majority of patients can tolerate penicillins after appropriate allergy evaluation [2-5]. Misdiagnosis of penicillin allergy is dangerous and associated with a myriad of adverse outcomes, including obligatory use of less-effective antibiotic alternatives, increased mortality and hospitalisation, higher healthcare costs, as well as development of multi-drug resistant microorganisms[6-11]. Unfortunately, with the severe lack of Specialists in Immunology & Allergy, the waiting time for a new case consultation in the public sector remains in the excess of 7 years. With the immense burden of false penicillin allergy labels and their severe consequences, more innovative and efficient delabelling approaches are urgently needed.

Inspired by Professor Lee's 'Hub-and-Spoke' model, our team developed the territory-wide Hong Kong Drug Allergy Delabelling Initiative (HK-DADI), featuring a nurse-triaged penicillin allergy evaluation protocol. The protocol has successfully shortened the waiting time for a routine penicillin allergy consultation in the public sector from over 7 years to around 1 year[12]. We conducted a comparative study to evaluate the effectiveness and clinical outcomes of HK-DADI compared to the traditional pathway, which was also presented at the Hong Kong Institute of Allergy Annual Scientific Meeting 2022.

The HK-DADI protocol for penicillin allergy

Under HK-DADI, patients referred to the Queen Mary Hospital for suspected penicillin allergy would be first interviewed by a trained nurse with a protocol-driven approach. After history-taking and counselling on penicillin allergy testing, patients would be triaged into 'low-risk' and 'non-low-risk' based on the pre-test likelihood of genuine penicillin allergy and the anticipated severity of potential reactions. Low-risk patients subsequently attended a dedicated nurse-led low-risk clinic where penicillin skin tests and, if skin tests were negative, drug provocation test would be performed in the same clinic session. Non-low-risk patients were referred for formal allergist review.

HK-DADI is highly effective and has led to better post-delabelling outcomes

A total of 312 patients completed penicillin allergy evaluation, among which 84 (27%) were evaluated via HK-DADI. Overall, 280 (90%) penicillin allergy labels were removed (i.e., delabelled).

Low-risk patients had significantly higher delabelling rate compared to non-low-risk patients (97% vs. 77%, p=0.01). Skin tests did not have additional diagnostic value in low-

risk patients, as all (100%) low-risk patients with confirmed penicillin allergies were diagnosed with positive drug provocation test following negative skin test; on the contrary, 83% of non-low-risk patients with confirmed penicillin allergies had positive skin testing and only 1 patient had positive drug provocation test following a negative skin test. No patients developed any severe/systemic reactions during evaluation. Upon a follow-up of 6–12 months after delabelling, 123 (44%) patients had suffered from infections which needed antibiotics, and 63 (23%) had used penicillin after delabelling. This proportion was significantly greater in those who were delabelled via HK-DADI than the traditional pathway (32% vs. 19%, p=0.03).

HK-DADI could minimise the need of unnecessary skin tests and cost-saving

Similar to previous studies, we found that skin tests did not add any diagnostic value among low-risk patients, and a nurse-led risk stratification could effectively minimise the need for unnecessary skin tests[13,14]. This has great benefits on saving potential costs, time, as well as valuable allergy specialist resources. Extrapolating the findings, based on the ratio of low-risk: non-low-risk patients and the cost of penicillin skin test (around HK$500 per person), implementation of HK-DADI could potentially save HK$345 per penicillin allergy label in skin test costs alone.

HK-DADI to become a new Hub-and-Spoke Model in Hong Kong

HK-DADI, a nurse-triaged evaluation protocol was effective in penicillin allergy delabelling. HK-DADI resulted in a higher rate of penicillin use after delabelling and could minimise the need of unnecessary skin testing in low-risk patients.

Based on these successes, the HK-DADI protocol has been received by the Hospital Authority as the first allergy Hub-and-Spoke model in Hong Kong. Since 2022, multiple “Spoke” HK-DADI centres have been established throughout Hong Kong and openly receive referrals from all across the territory. These Spoke HK-DADI centres are run by trained nurses and non-allergists to independently perform penicillin allergy delabelling, under the guidance and supervision by Allergists at the “Hub” (University of Hong Kong/Queen Mary Hospital). Penicillin allergy can now be evaluated through Hong Kong without the need for Allergist evaluation.

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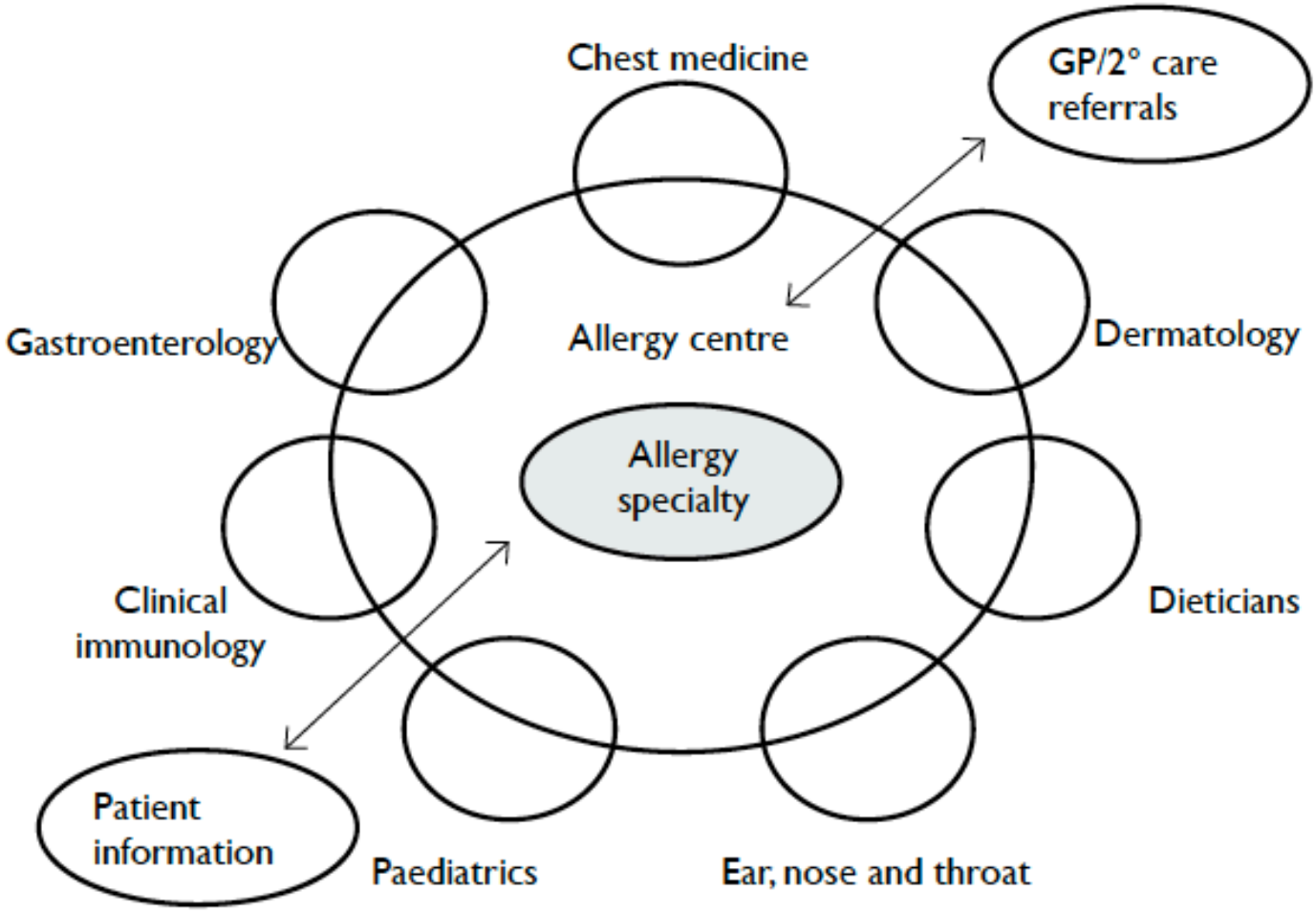
Figure 1: Hub-and-Spoke model for Hong Kong as first proposed in 2015[1]



Immunological disorders and vitamin D status: recent evidence

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Autumn 2022, after 3 yrs. of social distancing, quarantine and lockdowns globally, the Vitamin D (VitD) status of populations, adult and paediatric is questionable, especially from a previous level of insufficiency.[16,17] This is of great concern in start of the post-pandemic era as a hyper-hygienic environment and protection from air borne irritants/microbes in the recent few years may have supported naivety in the immune system especially in the young.

Calcitriol, the active form of Vitamin D (VitD) in the body, plays a pivotal role in innate and adaptive immunity. The immune-stimulatory and regulatory properties of VitD are essential to pathogen defense. Evidence also suggests deficiency may reduce immunity and skew the process towards allergies and autoimmunity.[3] An awareness of the pathophysiology of VitD insufficiency in auto-immune disorders and allergies would be beneficial for clinicians.

Auto-immune disorders and Vitamin D

Recent data suggests suboptimal VitD status as a risk factor for various Auto-immune diseases. Lower Vitamin D levels have been documented in auto-immune Hashimoto's Thyroiditis and Inflammatory bowel diseases (Ulcerative Colitis, Crohn's and IBS).[3]

In separate clinical trials lower levels of VitD were reported in children with Kawasaki's disease, and Juvenile Idiopathic Arthritis. Deficient levels and reducing of levels in winter correlated with severity of the diseases.[14,18]

In adults with Eosinophilic Oesophagitis, a disease presenting as dysphagia with distinct IgG4 mediated oesophageal epithelial pathology, VitD levels were inversely associated with severity and epithelial histopathology. Reversal of pathology including reduction of IL-13 induced allergic inflammation, epithelial hyper-proliferation, improved barrier permeability with reduction of the dilated intercellular spaces was documented on supplementation.[4,6]

Vitamin D status correlated with the development and severity of Rheumatoid Arthritis, SLE and Multiple sclerosis (MS). One study suggested the support of Vitamin D in pain management in RA especially in combination with TNF-Alpha inhibitors and a reduction in the inflammatory component of MS.[3]

Improvements in IBD on supplementation trended towards reduced inflammation, improvement of the intestinal barrier and modulation of the gut microbiota. Trial data showed patients with normal VitD levels receiving anti-TNF alpha medication had increased odds of achieving remission in 3 months vs those with low levels 2.64 (95% CI 1.31–5.32, $p = 0.0067$).[10]

Allergies and Vitamin D

It is well established that 25(OH)D deficit is associated with increase allergic sensitization to foods chronic and spontaneous urticaria, atopic and contact dermatitis and asthma in the paediatric and adult population. Table 1 summarises recent evidence.

Immune modulation and Vitamin D: a glimpse into present day evidence

Clinical, invitro and epidemiological data suggest a tendency to Type 2 Immune response disorders in VitD insufficiency states. Table 2 summarises recent evidence on the role of Vitamin D in immune modulation. VitD supplementation studies show a move towards a more tolerogenic Th2 response.

Urgent need for monitoring and research of Vitamin D levels

As further evidence mounts on the pivotal role of an optimal VitD Status (⩾ 30ng/ml or 75nmol/l) in maintaining an optimal balanced immune response, there is urgent need for local clinical research. To ensure best practice at a clinical and public health level, an audit of Vitamin D levels of patients and population in relation to health and disease especially in allergies and auto-immune disease is warranted. Timely identification of Vitamin D insufficiency states may support therapeutics and public health.

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Table 1: Allergic diseases in relation to Vitamin D Status

Allergic Disease	Documented evidence in relation to VitD
Atopic Dermatitis	low level of vitamin D was correlated with the severity of AD, which was dependent on IL-17A.Improvement on Supplementation.[5,12]
Asthma	24.6% asthmatics (20-30ng/ml Vit D , 3.4% <20ng/ml. [1]
Allergic Rhinitis (AR)	Lower VitD level in AR vs controls (p=0.014). Significant negative correlation between IgE and vitamin D levels in the allergic rhinitis group (P = .028, r = −0.246).[8]
Chronic Urticaria & Chronic Spontaneous Urticaria	VitD3 supplementation reduced symptom severity.[15]
Eosinophillia	Vit D3 decreases (IgE) synthesis and increases expression of IL-10.[1]
Food Allergy	VitD level lower than 15ng correlated with higher sensitization. Reduction of CD69+ and CD4+ T cells can help reduce food allergy.[9]

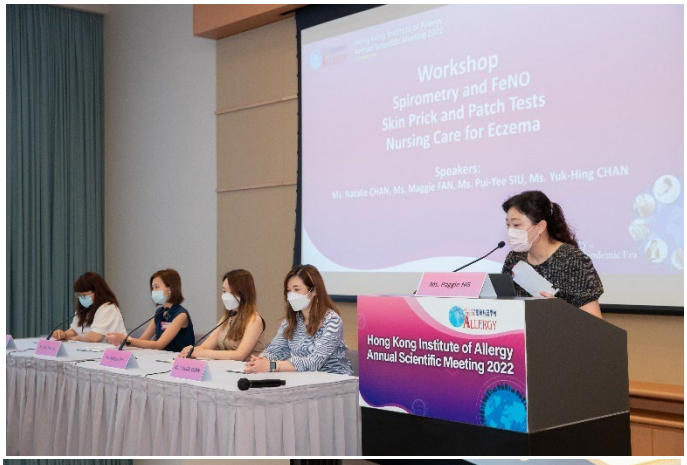
Table 2: Role of Vitamin D in Immune Modulation – a few points in relation to allergies and immune disorders[3]

1. Macrophages, T cells, dendritic cells, monocytes and B cells have VitD receptor sites and the VitD activating enzyme 1-α-hydroxylase suggesting the role of VitD in their regulation
2. Modulation of T cell activation mainly inhibition of Th1 cells and reduction in organ-specific auto immunity via inhibition of TH17 cells.
3. Modulation of phenotype and functioning of dendritic cells.
4. Enhances production of defensin β2 and cathelicidin key antimicrobials.
5. Downregulates inflammatory cytokine and reactive oxygen species, Decrease in IgE synthesis and increase Il-10.[1]
6. Attenuated B cell proliferation, differentiation and immunoglobulin production.
7. Manipulates monocytes and dendritic cells at different levels enabling them to exert tolerogenic activities.

Hong Kong Institute of Allergy | Annual Scientific Meeting 2022

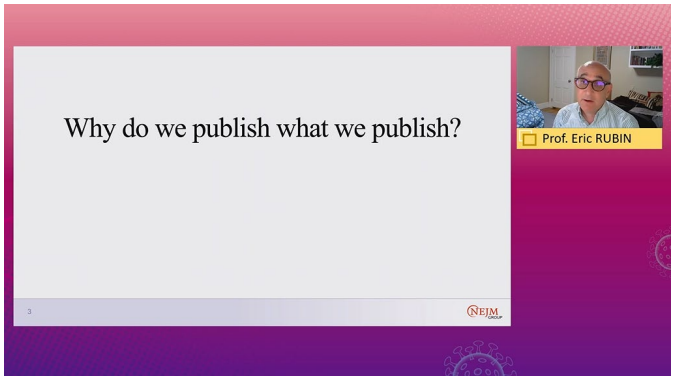
Date: 25 September 2022 (Sun)

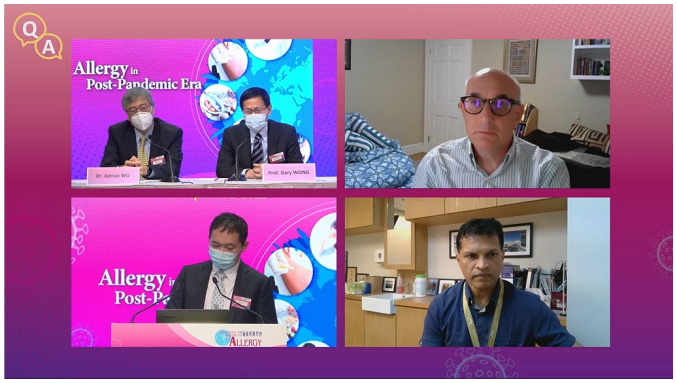
Workshop



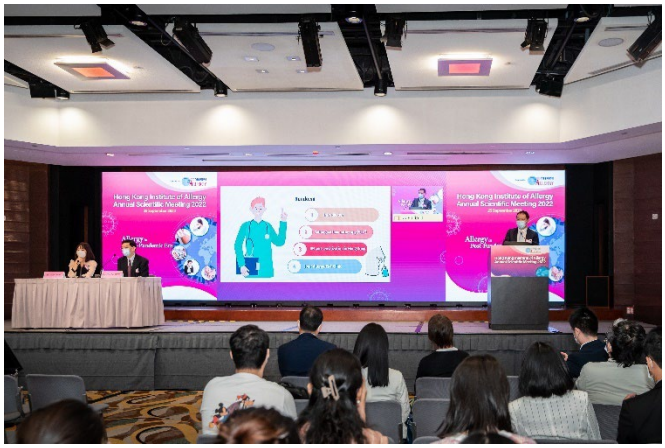
Opening Address

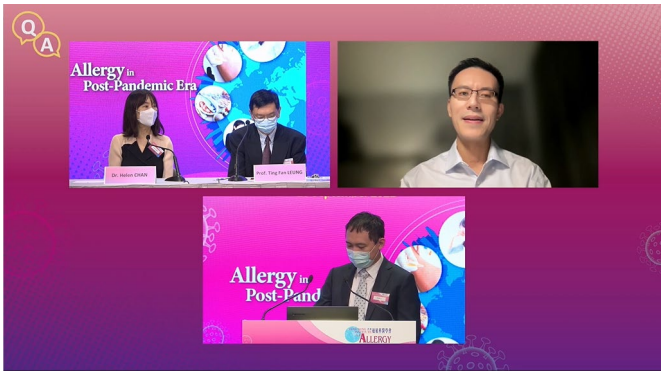
Symposium 1: Era After COVID-19 Pandemic



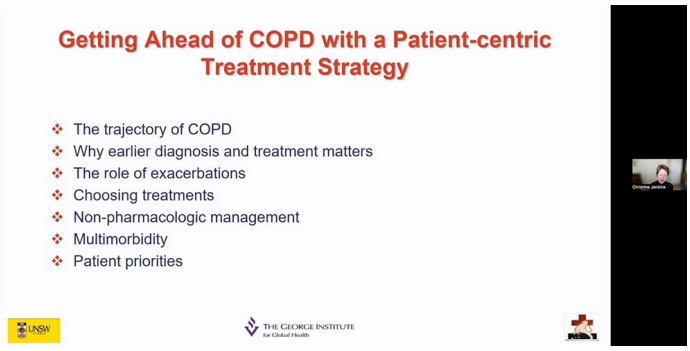


Symposium 2: Food and Nasal Allergies

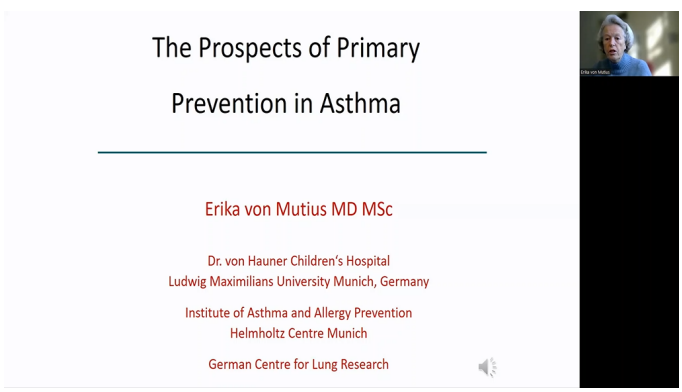




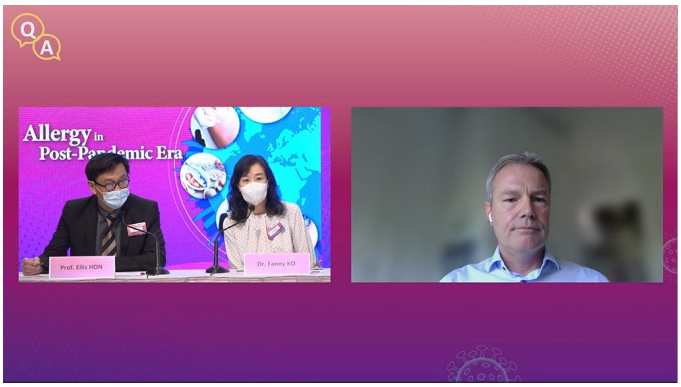
Symposium 3: Update on Management of Respiratory Diseases



Plenary Lecture



Symposium 4: Biologics for Allergic Diseases



Closing Ceremony

Memorable Moments

Overseas Meetings

APAAACI 2022 PSAAI@50
5 - 8 December 2022 / Manila, Philippines (https://www.apaaaci.org/2022)

EAACI 2023 (European Academy of Allergy and Clinical Immunology 2023)
9 - 11 June 2023 / Hamburg, Germany (https://eaaci.org/events_congress/eaaci-congress-2023/)

ERS 2023 (European Respiratory Society (ERS) International Congress 2023)
9 - 13 September 2023 / Milan, Italy (https://www.ersnet.org/congress-and-events/congress/)

CHEST 2023 (The American College of Chest Physicians Annual Meeting 2023)
8 - 11 October 2023 / Honolulu, Hawaii (https://www.chestnet.org/Learning-and-Events/Events/CHEST-Annual-Meeting)

ACAAI 2023 (American College of Allergy Asthma and Immunology Annual Scientific Meeting 2023)
9 - 13 November 2023 / Anaheim, California, USA (https://annualmeeting.acaai.org/)

Local Meeting

Hong Kong Allergy Alliance Educational Symposium on Allergy in Hong Kong
26 February 2023