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Message from the Editors

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The springtime is a time of renewal and hope, especially after the difficult year we've all had due to the pandemic. We can look forward to being able to meet, dine and travel with our friends and family, enjoying the world in its fullest form.

In memory of the late Professor Tak Hong LEE, a world-renowned authority on allergy and respiratory medicine and the inaugural Director of Hong Kong Sanatorium & Hospital Allergy Centre from 2012-2022, a naming dedication ceremony for the HKSH Lee Tak Hong Allergy Centre was held on 2 April 2023. I was privileged to be invited to give a short speech on behalf of our Institute, HK Allergy Association, and Hong Kong Allergy Alliances in thanking Lee's family and many co-workers.

In this issue, we welcome Dr. David C.M. YEUNG to join us as new ENT Section Editor. He shares his thoughts on endotyping of chronic rhinosinusitis in Asia. Endotyping of CRS has an implication on choices of biologics and other therapy and respective responsiveness.

Our regular contributor and Associate Editor Dr. Agnes S.Y. LEUNG always gives us good treat with her succinate and practical tips for daily allergy practice. This time her short review on egg and milk ladders which are initially intended for non-IgE- mediated allergies, are increasingly being modified for IgE-mediated allergies as an alternative form of dietary advancement therapy (DAT), is another very useful piece of work.

How can the lab help to diagnose an allergy? The forthcoming title offered by Lab Immunologist from QMH Dr. Elaine Y.L. AU who leads us inspecting through her tool box and armamentarium that clinicians may find them well supported for managing clinical conundrum.

Fish free diet for fish allergy subjects may lead to potential nutritional deprivation. The relevancy of fish oil supplementation for DHA/EPA and Omega 3 is a frequently asked question. Dr. Sonal HATTANGDI-HARIDAS has given a brief review on omega-3 supplementation depicting the risks, benefits and options from a nutritional scientific perspective Ms. June K.C. CHAN helps us with "Ask the Expert" section through interactive exchanges with Dr. Patrick C.Y. CHONG on introduction of potential allergenic foods in infancy through lens of impetus for allergy prevention.

Meeting Highlights captured Hong Kong Allergy Alliance Educational Symposium on Allergy in Hong Kong which themed "Improving Allergy Care Standard through Trans-disciplinary Collaboration". It was well attended on Sunday 26 February and also an important legacy of Late Professor Tak Hong LEE who originated the idea and grafted the programmes. Special thanks went to all speakers Drs. Elaine AU, Alson CHAN, Valerie CHANG, Gilbert CHUA, Fanny KO, Agnes LEUNG, Donald LI, Axel SIU, Zion TO and Adrian WU who have graciously donated their time, efforts and good will to juggle with the tight schedules. MIMS secretariat Ms. Catherine LAM and Ms. Sigourney LIU have been proficient in supporting the event.

The most expected upcoming event in 2023 will be our Institute's biennial Hong Kong Allergy Convention scheduled on 7-8 October, at Hong Kong Convention & Exhibition Centre. A truly flagship CME activity for Allergy and related specialities, is keenly supported by EAACI, BSACI, and ACAAI with a stardom of eminent speakers. Don't miss it. Please mark your calendar now.

Until next time, take care in light of the uptick of COVIDs and remerging old respiratory viruses claiming "immunity debts" from old, young and frail.

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

Speech at the Naming Ceremony of HKSH Lee Tak Hong Allergy Centre

Dr. Tsao, Chairman of Hospital Management Committee and Deputy Superintendent,

Dr. Chan, Chief Medical Officer of HKSH Medical Group and Deputy Superintendent.

Lee's family, Ladies and gentlemen, it's my absolute honor to speak a few words on this special occasion. On behalf of people whom Tak had been closely worked with, namely, the staff of Allergy Centre, the Council of HKIA- a professional organization; Exco committee of Hong Kong Allergy Association-a charity and patient support organizations; Hong Kong Allergy Alliance- a Think Tank for policy blueprint to improve allergy service and training infrastructure, I'd like to pay tribute and express my gratitude to Tak and his family.

First of all, it's a tremendous pleasure and privilege to have known Tak for more than 10 years during which I witnessed his enormous contribution to Hong Kong Allergy Community and medical science. I have always admired his scientific curiosity, driven with determination but always accompanied by patience and pleasant demeanor. We have lost a gentle giant colleague, the most influential leader in Allergy of our times. Many of us are yet to recover from his sudden departure. Tak 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 our community.

Tak retired from his Professorial post at King's College London and as Director of the Medical Research Council - Asthma UK Centre in 2011. Since then, He returned to Hong Kong and had devoted himself to HK allergy and unified a distinguished team of colleagues to transform the professional credibility and public perception of the specialty.

The ground breaking **Allergy Centre** which he established at HKSH Medical Group (HKSH) in 2012 stands as a great example of his untiring work to serve patients and he did so in part by building an exceptional team around him. To name a few, Dr Alson Chan, Manager Helen, Senior Nurse Lik, Senior Dietician June, Nurse leaders Wing-Luen, Gigi, ChingChing, Sabrina, Kelly, Wendy. By the way, the Allergy Team has grown and welcomed two new-borns of our staff back-to-back in last 4 months. A huge blessing to this big family! Tak in a better place would be joyous to learn the great news. As a newcomer, I immediately observed that there is a sense of purpose, mutual respect, teamwork, efficiency, and always, when appropriate, a sense of humour and humanity.

In last months, patients came back praising how Dr Lee had transformed their lives with his calm, kind, gentle, thorough and always professional presence which was immediately reassuring regardless how complicated the allergy problem was. Patient after patient's testimonies vividly depicted how Tak was indefatigable in his efforts to help each of them, often thinking well beyond the box and well beyond office hours in order to find treatments for complex allergy issues. His magical healings reached to tens of thousands of allergy suffers. He possessed perhaps the greatest skill of a successful clinician: he listened to his patients and he cared deeply about the patient as a whole. Improving the quality of life of his patients was foremost in his mind at all times.

Many patients of and visitors to HKSH who have never heard of Dr. Lee benefitted from his work as he, together with our senior dietician June Chan, created an Allergy Menu so that people with food allergies, whether inpatients or visitors eating in the canteen, could order a meal knowing that it would be safe for them.

From a wider community perspective, Tak actively engaged colleagues from the universities, HA and the private sector in a cohesive partnership for the benefits of HK's community. With the gracious presence of Dean of HKU Medical School Professor CS Lau, HKIA incumbent President and CUHK Medical School Professor Garry Wong, Founder of HKIA and Past President of HKIA Professor Christopher Lai, HKU Medicine Division Chief of Rheumatology and Immunology Dr Philip, they join me to testify Tak's altruistic visionary commitments. Tak 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 practice guidelines, created an active subcommittee structure; and launched an informative newsletter, webpage and social-media platforms. Tak attracted substantial sums of uncommitted funding to HKIA. He emphasized the need for rigorous governance and had written detailed formal operational procedures 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 – **Hong Kong Allergy Association** - to encourage public engagement and outreach. Tak officiated the opening of a new patient education resource centre in downtown of Yau Ma Tei in 2017. 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 HK Institute Allergy in 2021.

Over the years as I came to know him and his family better, attending his daughter Jackie's wedding, dinning with him on many occasions before pandemics, over the tables, he would speak from time to time about his family. His face would light up as he described with delight and pride Jackie's prowess in baking and the success of Adrian in playing cricket and adorable grandsons Obie and Remi's cheeky anecdotes. As much as I miss him immensely both as an exceptional colleague and great friend, I can only imagine what his loss means to his family and all who loved him and worked with him.

HKSH's Hospital Management Committee's Naming Dedication is the best benevolent gesture in appreciating Tak's visionary leadership, passion and dedication. Seeing the Lee's Family and his Allergy Team gathering here today in honouring Dr Lee's life with great pride, is perhaps one the most heart-warming scenes that I have ever experienced. Tak's elaborated service was truly a fulfilled journey, a lucrative gift to his hometown. He started from scratch in drawing board until seeing the fruition. The drive of him has been to identify a wicked problem, recover the evidence and research, and then develop policies and practical strategies that could be implemented for societal good. **Professor Lee Tak Hong has reflected the lofty aspirations of Founder of this Hospital Dr Li Shu Fan and his famous quote "… to leave the world a little richer than I found it".**

Tak's legacy will live on for generations to come. For those of us working under the auspice of new name **HKSH Lee Tak Hong Allergy Centre** will continue strive our very best to serve allergy community well and we will do Tak proud.

Thank you very much!

By Marco HO – Chairman of HK Allergy Association, Co-convener of Hong Kong Allergy Alliances, Immediate past president of Hong Kong Institute of Allergy

Date 2 April 2023

Endotyping of chronic rhinosinusitis in Asia

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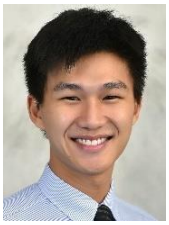

Chronic rhinosinusitis (CRS) is the persistent inflammation of the sinonasal mucosa arising from a complex interplay between host and external factors. The prevalence of self-reported and CRS diagnosed by physician was 10.9% in Europe and 11.9 in the United states.[1] In a national surgery in China, the prevalence of CRS was reported as 8%, ranging from 4.8%–9.7% in different cities.[2] CRS can be classified into primary or secondary, anatomical locations, localized or diffuse bilateral, endotype dominance, and phenotypes.[3]

The endotyping of CRS is an emerging field of research in the western countries. The classification of the disease by endotypes would be into two broad categories: type 2 or non-type 2. These categories would direct the use of therapy in addition to common treatments of nasal saline irrigation, intranasal steroids or functional endoscopic sinus surgery. For type 2 disease oral steroids or biologics can be an additional therapy. For non-type 2 disease, long term antibiotics as well as Xylitol rinses can be considered. Symptomatology of type 2 disease includes bilateral nasal obstruction, smell loss, blood and mucosal tissue eosinophilia with elevated IgE levels, concurrent NSAID-Exacerbated Respiratory Disease, asthma, and atopy. [4]

In the East Asian population with CRS, prevalence of type 2 endotype ranged from 20-60%. The Asian population also demonstrated a more prevalent mixed type 1 and 2, or type 2 and 3, which is more rarely seen in the United States of 26%. Type 2 inflammation are classically characterized by cytokines such as IL-4, IL-5, and IL-13, and non-type 2 characterized by neutrophilic inflammation, elevated IFN-γ, IL-17α- and IL-6.[5 6] Several biologics have been used in the treatment of CRSwNP, such as Dupilumab, Omalizumab, and Mepolizumab, mainly targeting anti-type 2 factors, such as anti-IgE, IL-5, and IL-4Ra.[7] The high longer-term recurrence rate of nasal polyps up to 60% after endoscopic sinus surgery would support the pursuit of further treatment options.[8] It was also demonstrated that CRS patients without nasal polyps (CRSsNP) patients in the United states are 30 – 50% type 2 dominant, which suggest that an endotype approach can be the future direction for biologics rather than a phenotype approach.[5]

Recent work by Nakayama et. Al. compared a Caucasian and Japanese cohort to illustrate inflammatory characteristics between these racial groups and geographics.[9] In this study, 8 Caucasian patients with CRSwNP were recruited from Stanford University and the University of Colorado, and 9 Japanese patients with CRSwNP who were of Asian ethnicity and born and raised in Japan were recruited from Dokkyo Medical University in Japan. The control patients had undergone skull base surgery or endonasal surgery for anatomic abnormalities but did not otherwise have sinonasal or upper airway inflammatory diseases. Despite numerous previous studies reporting major differences between Caucasian and East Asian nasal polyps, there were no disparities noted on the transcriptomic screen. The expression analysis of each endotype representative type 1 (IFNG), type 2 (CLC, IL5, and IL13), and type 3 (CSF3 and IL17A) inflammatory cytokines showed no significant expression differences between Caucasian and Japanese nasal polyps, except for IFNG. Other prominent inflammatory transcript expression was identified to be associated to the type 2 dominant cases with droplet-based single-cell RNA sequencing, which are C-C motif chemokine ligand 13 (CCL13) and CCL18 in M2 macrophages, as well as cystatin SN (CST1) and CCL26 in basal, suprabasal, and secretory epithelial cells. The study showed the proportion of the type 2 endotype being more prevalent in the Caucasian cohort (63.0%) than in the Japanese cohort (41.9%). This difference in type 2 was statistically significant ($P = 0.034$). Reproducibility of the study findings and results was confirmed by quantitative PCR in an independent validation set of 46 Caucasian and 31 Japanese patients. This study concluded that the nasal polyps from Caucasian and Japanese racial groups harbor the same 2 major endotypes but was present in different ratios in this cohort of CRSwNP. Distinct inflammatory and epithelial cells contribute to the type 2 inflammatory profiles were also observed.

Endotyping of CRS has a bearing on responsiveness to biologics and steroid therapy. This is especially important for patients where conventional medical therapies and surgery has failed. Recent advances in deployable devices such as absorbable steroid eluting sinus stents could be beneficial for endotype guided selection of cases of CRS.[10] With new studies on endotyping of CRS with or without nasal polyps in the East Asian population, more treatment options could be tailored for CRS cases refractory to conventional management.

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Current state of dietary advancement therapy

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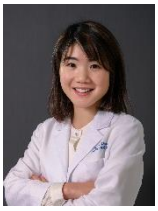

Traditionally, the standard approach to managing food allergies involves full allergen avoidance while waiting for natural tolerance to develop. For egg allergy, it is estimated that around 50-80% will outgrow egg allergies by 6 years of age, whereas only around 30% will outgrow their peanut allergies.[1,2] Until recently, research indicates that reintroducing **egg and milk** in a baked or heated form promotes acquisition of oral tolerance, and serves as the foundation of egg and milk ladders.[3] Egg and milk ladders, which are initially intended for non-IgE-mediated allergies, are increasingly being modified for IgE-mediated allergies as an alternative form of dietary advancement therapy (DAT). More recently, studies have shown that reintroduction of allergens at subthreshold levels, in patients who are not "highly allergic" – those who are reactive at a high threshold and have not had severe reactions, can be effective in raising the allergic threshold and improving safety.[4] These patients often do not benefit from the common practice of strict allergen avoidance, an approach that often imposes burdens to patients and caregivers.

DAT for egg allergy requires gradual reintroduction of egg, from baked to almost raw form of egg, in a stepwise manner. Heating eggs at high and prolonged temperature and interaction between proteins, fats and sugars, also known as the "matrix effect", reduce the allergenic potential of the egg allergen.[5] A recent report by Cotter et al showed that majority of egg-allergic children (n=29) who followed the Irish Food Allergy Network (IFAN) guidelines in gradually escalating exposure to egg were able to tolerate step 3 of the egg ladder (e.g. scrambled egg) safely without adverse reactions within a year.[6] This applied to both patients with egg allergy only and also those with multiple food allergies. Children were commenced on egg ladder from around 18 months old, and most achieved tolerance before 3 years of age. No one experienced severe allergic reactions while receiving the planned egg products from the IFAN egg ladders, and all procedures were home-based with remote guidance provided by experienced personnel from the allergy clinic. This new strategy in managing egg-allergic children was shown to be particularly helpful amidst the COVID-19 pandemic.

A culturally adapted egg ladder for use by Chinese patients and families were developed by the team at Allergy CUHK (Figure 1). Patients who are deemed suitable to be commenced on egg ladder are usually those without a history of anaphylaxis, with well-controlled asthma and families who could follow instructions for egg ladder escalation and anaphylaxis action plans. On the contrary, egg-allergic children who previously had an anaphylactic reaction to baked egg and those with poorly controlled asthma should be advised against the intake of any form of eggs at home without medical supervision. Although food ladders show increasing promise, they are not without risk. Patient-specific characteristics often impact tolerance and safety to food ladders on a daily basis. Obtaining informed consents from parents or guardians are essential before commencing patients on food ladders. Further details about the shared decision-making process can be referred to a previous article in the HKIA e-newsletter: https://www.allergy.org.hk/eNewsletter/e-Newsletter2022spring.pdf

Besides, researchers have recently experimented on introducing subthreshold level of peanuts at home in children who were "low-dose tolerant, high-dose mild".[7] These young children took one **peanut** three times per week and doubled the amount at home until reaching the dose that they last tolerated on the initial oral food challenge (OFC). Most children were shown to tolerate the full dose of peanut challenge after 6 months, and a subset even attained sustained unresponsiveness (stopped peanuts for 6 weeks and pass the OFC again). In a similar way, OFCs in stepwise manner are well-established in Japan.[8] In this study, patients who were **egg, milk and wheat-allergic** were invited to first undergo the low-dose OFCs to identify whether they could tolerate 213mg egg, 850mg milk and 372mg wheat. If they passed the challenge, they were instructed regular consumption of the allergens below the tolerated dose. Within a year, they would return for the medium-dose OFCs that contain 1550mg egg, 3400mg milk and 2600mg wheat, and within 12 months, another set of full-dose OFCs (6200mg egg, 6800mg milk and 5200mg wheat) would be performed. This 3-step protocol appears to be practical, well-tolerated and safe, whereby most patients could regularly consume the low or medium dose of the allergen safety at home.

Food allergy management is a constantly expanding area. It is not wrong to continue advising patients on complete allergen avoidance, which is a reasonable and safe approach. However, it is also a prime time for us to consider whether these novel strategies in permitting subthreshold intake of dietary allergen can be a feasible and safe way to manage food allergies in our locality.

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Source:
https://www.allergycuhk.org/
http://bit.ly/3JAvgkX

How can the lab help to diagnose an allergy?

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Allergies refer a number of conditions caused by hypersensitivity of the immune system to typically harmless substances in the environment. Allergy tests are commonly employed to identify causative allergens. There are a range of laboratory assays to facilitate the workup, however, a good clinical assessment is crucial for directing the choice of investigations and results interpretation.

Biomarker for allergic reaction

The presentation of allergic reactions varies with allergens and susceptible individuals. The clinical presentation could range from mild cutaneous manifestation to anaphylaxis. Often, the diagnosis is made clinically without a biomarker for confirmation of the event occurrence, except for the use of tryptase in anaphylaxis workup. Tryptase is mast cell mediator, that degranulated upon mast cell activation. The current commercial assay (ImmunoCAP, Thermo Fisher, Uppsala, Sweden) measures total tryptase with the cutoff of >11.4 µg/L considered as a positive result. However, increases in tryptase level below this cutoff could still be clinically significant, and interpretating the results in pairs with comparison of the sample taken during the event and baseline, has been shown to achieve better sensitivity.1 In this algorithm, acute tryptase (within 30-240 mins from the event) and baseline tryptase (24 hrs after the event) was compared. Acute increases of ≥20% + 2 ng/mL (20 + 2 rule) over basal serum tryptase (BST) was considered as significant mast cell degranulation events. Alternatively, a recent publication has suggested the use of acute tryptase/BST ratio of >1.685 for anaphylaxis diagnosis2. In general, tryptase elevations were more often encountered in drug and venom anaphylaxis than food related anaphylaxis.

IgE allergy diagnostics

Though total Ig E is commonly arranged during the assessment of atopic disorders, elevated total Ig E is not specific for atopy diagnosis. It may be increased in a range of conditions, such as bullous skin diseases, parasitic infestation, allergic bronchopulmonary aspergillosis, vasculitis (e.g., Eosinophilic granulomatosis with polyangiitis), hematological malignancies (e.g., Ig E myeloma, Hodgkin lymphoma), primary immunodeficiency conditions (e.g., Hyper Ig E, Wiskott Aldrich syndrome), etc. Though lowish result may help clinicians to consider non-atopic causes, normal finding does not necessarily exclude allergic disorder. Skin test and allergen-specific Ig E (SIg E) test are better options as dedicated workup for allergy disease.

Skin prick test is widely used in allergy workup, that it is quick (results available within 15-20 minutes) and can be done as an office procedure. It is a sensitive test that is applicable in a wide range of allergens. However, it requires expertise to perform and interpretation. Moreover, some patients may have difficult skin conditions (e.g., severe eczema, dermatographism, psoriasis) or taking medications (e.g., anti-histamine, tricyclic anti-depressants), that make skin testing not feasible. SIg E assay complement skin test in the allergy assessment. SIg E assays are available to detect sensitization to a variety of allergens, (food, insect venoms, environmental allergens, latex, drugs, etc), but the performance varies with allergens. Overall, the in-vitro test is less sensitive than skin test assessment. There are several assays platforms for checking SIg E, that varies in assay designs. Hence, if consistency is preferred for serial monitoring, checking the test with the same assay platform during follow up is suggested.

Results of SIg E provide information on the allergen sensitization status of the individual. However, it's important to note that sensitization not always correlate with clinical reactivity, that a positive result is not diagnostic on its own. In general, the higher the SIgE level, the higher the likelihood of symptomatic allergy. It is possible to have positive sensitization but without clinical symptom, that a false-positive rate of greater 50% has been reported in population-based studies in food allergy (3-5). In addition, the level of SIgE does not correlate with the severity of clinical symptoms. Hence, dedicated clinical assessment is crucial for patient management and prevent unnecessary dietary exclusions, social restrictions, and anxiety, that negatively impact on patients' nutrition and quality of life.

In recent decade, component resolved diagnostics has revolutionized the workup in the field. Instead of testing SIg E level against the whole allergen extract, SIg E response against allergen component molecules is being measured. The new advances help to improve the assay analytical sensitivity, useful for risk prognostication, provide additional information on cross reactivity and marker for primary sensitization source 6. The information is helpful in the planning and decision of immunotherapy. Other advances in allergy diagnostics include the availability of multiplex testing, that a single test provide sensitization profile with a number of sIgE results. These multiplex assays most commonly available as panel-based microarray assays e.g., ISAC, ALEX, Microtest etc. The panel size varies with different assay options. While some large panel may include items up to

hundreds of allergy extracts and allergen components in a single assay, the allergens included are by no means exhaustive. Hence, one needs to be aware of the assay performance and limitations, in particular, if the suspected allergen is included in the assay panel. In general, multiplex assay provide a broad profile with minimal blood volume required, and hasten the workup compared to traditional serial testing. It is useful in the workup of complex sensitization cases, and in cases without a clear allergen identified, e.g., in recurrent idiopathic anaphylaxis. However, results interpretation could be challenging, especially when unexpected positivity arises. Hence, specialist input is often required. The test should not be used as a general screening in an indiscriminate manner. Overall, the sensitivity of individual allergen item within the panel assay is less compared to traditional singleplex platform, and results in microarray are provided in semi-quantitative manner. Therefore, traditional singleplex platform is preferred if test sensitivity is a concern or if serial monitoring is needed.

Apart from sIgE assay, the application of cell function tests in allergy workup is gaining popularity. For example, the use of basophil activation test in peanut allergy, has been shown to minimize the need of oral food challenge7. Though double-blind, placebo-controlled food challenge is the gold standard for food allergy diagnosis, it is time-consuming, costly, and has the potential risk for anaphylaxis. Hence, tools that facilitate risk stratification before decision to challenge test is desired, and basophil studies are promising. However, basophil testing requires fresh sample and around 10-15% of the general population have non-responder basophils yielding inconclusive results. Lately, some research groups investigated the utility of studying mast cell activation in allergy workup. By employing cell lines or primary human blood-derived mast cells (MCs) generated from peripheral blood precursors, some of the limitations of basophil testing is addressed. Preliminary data in peanut allergy cohort is promising. In one publication, it even outperformed skin prick test, specific Ig E test, and basophil activation test 8. Nevertheless, the assay is technically demanding, especially in the aspect of mast cell culture. Further studies are required to explore its role in routine clinical setting, as well as its application in other allergies. At the moment, the mast cell assay is a research-based assay, that is only available in some special research centers. Overall cell-based assays applications are limited by its availability and issues of standardization across different laboratories.

Non-Ig E mediated allergy workup

Overall, in-vitro assays options are relatively limited in non-Ig E mediated allergy. Nevertheless, some of these in- vitro tests do play an important role, for example, the use of lymphocyte transformation test (LTT) and Enzyme-linked immunospot (ELISPOT) assays, in the workup of severe cutaneous adverse drug reactions. Other assays, such as pharmacogenetic test (e.g., HLA genotyping), is now the standard of care for hypersensitivity risk assessment in certain drug prescription items.

The field of allergy diagnostics is rapidly evolving, with increasing options. Advances in component resolved diagnostics and cell function assays are promising, that facilitate the practice of personalized medicine in allergy disease management. However, knowing the assays performance and limitations, with careful test selection and results interpretation, is crucial to translate these advances into better patient care.

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IgE-mediated fish allergies and omega-3 supplementation: risks, benefits and options

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Fish allergy inflicts 7% of the global paediatric population and is a growing challenge. Symptoms may appear on ingestion, skin contact, inhalation of fish protein antigen, and range from urticaria, gastric symptoms to anaphylaxis. Symptoms may persist into adulthood. Traditional approach to managing this allergy is fish avoidance and treating symptoms.[2]

Nutritional value of fish in a traditional fish eating population: Supporting the fish free diet

Fish is an essential source of Omega-3, vitamins A, B group and D3, ferritin, potassium, magnesium, iodine and fibre. Much can be supported through dietary advice and supplementation yet Omega-3 supplementation commonly derived from fish oil remains elusive.[8]

Essentiality of dietary n-3 polyunsaturated fatty acids (n-3 PUFAs) commonly known as Omega-3 and the concern of fish oil supplements: A double-edged sword

The mammalian body cannot synthesize n-3 PUFAs and is dependent on dietary intake for its needs.

n-3 PUFAs are of 2 types: the long chain 18 Carbon fatty acid with 3 double bonds (α-linolenic acid [ALA]) and the very long chain with 22 carbon with 5 and 6 double bonds eicosapentaenoic acid [EPA]), docosahexaenoic acid [DHA] respectively. n3-PUFAs are associated with anti-inflammatory responses including limiting neutrophil infiltration, inhibiting pro-inflammatory cytokine production via inhibition of nuclear transcription factor NF-κB.[4]

EPA & DHA are essential for normal brain, retina development, reducing risk of allergies and in maintaining cardio-metabolic health. A critical component of each cell membrane including epidermis, DHA enriched cells are documented to have higher resistance to becoming carcinogenic and atopic and an improved response to chemotherapy.[6,12]

Various neuro-psychiatric disorders, ADHD have documented benefits from Omega-3 consumption. Nutritionally considered critical during pregnancy and early childhood, supplementation has shown to improve attention scores and reduce systolic blood pressure.[3]

The healthy benefit of the ideal n3:n6 PUFA dietary ratio

n-6 PUFAs such as Archidonic Acid (AA) derived from Linolenic Acid (LA), higher in corn and soybean oil are associated with inflammatory responses. n6 and n3-PUFAs are competitive in bio-absorption.

Limiting n3-PUFAs in the diet may skew the ideal dietary ratio of n6:n3 (1:1 or 1:2) specifically AA:EPA. This ideal ratio is documented to: limit production of the inflammatory Eicosanids (that affect Th2 Lymphocytes and ILC2 cells), attenuate the risk and development of various cancers (via apoptosis modulation) and cardiovascular disease.[6,11,12]

Fish oils and alternatives in a fish free diet: Recent evidence

Available evidence strongly favours a milieu interior enriched with DHA and EPA and maintaining a healthy n6:n3 index to support immediate and long term health. Consumption of n-3 LC-PUFAs through a diet rich in certain microalgae, free range-grass fed ruminants and preformed n-3 derivatives is suggested.[12]

While Pecoraro et al 2022, documented an absence of serious adverse events related to the fish oil based Omega-3 supplementation in children with fish allergies, other studies document concerns on quality control of purification and contamination of fish oil in commercial supplements.[7,8]

Intake of ALA fortified foods show limited conversion (10%) to the bioactive EPA/DHA and negatively affected the n6:n3 ratio due to bio-absorbability issues. Echium plantagineum, Buglossoides arvensis, and Ribes sp. sources of Stearidonic Acid (SDA) have better convertibility than ALA. Microalgae and thraustochytrids directly supply DHA/EPA and are a good vegan source.[9]

The 'Omega-3 index' (EPA + DHA (O3I)), used to compare n-3 status, metabolic conversion and bioavailability found microalgal supplementation superior to flaxseed or echium seed oil.[5]

Attention to Omega-3 status in patients on fish-free diets

Evidence suggests, timely heed must be paid to the Omega-3 levels and n3-n6 ratio in all diets especially Fish-free diets. Evidence based dietary advice and supplementation may benefit immediate and long-term mental and physical health in the paediatric and adult population. Further study into quality and dosage of Omega-3 supplementation in allergies is urgently needed.

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Ask the Expert

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Introduction of potent foods in infancy

Introducing babies to solid foods is an exciting milestone in their development. It's a time for exploration and discovery as they learn to eat and enjoy new flavors and textures. However, solid introduction can also lead to worries and frustration, especially with potentially allergic foods. In this article, we have invited Dr. Patrick Chong to discuss the importance of solid feeding and allergy prevention and provide tips for introducing allergenic foods to your baby.

Q: What are the current guidelines on infant solid introduction?

A: There is a consensus from the American Academy of Allergy, Asthma and Immunology (AAAAI); American College of Allergy, Asthma and Immunology (ACAAI); and the Canadian Society for Allergy and Clinical Immunology (CSACI) about solid food introduction as a strategy for primary prevention of food allergy in 2021.(1) Complimentary food should be introduced to infants at around 6 months old without delay. Appropriately textured solid food, including peanut containing food and cooked form of egg, should be introduced to infants who are developmentally ready at around 6 months old but not earlier than four months. Once the complimentary food is introduced and tolerated by the infant, it should be maintained as a regular diet. A diverse diet is also recommended.

Q: It is often found that parents are introducing the potentially allergic foods such as peanut or shellfish cautiously slow, sometimes even leading to delayed introduction. Do you have any pro-tips on introducing these foods?

A: Parents worry about the risks of allergy for introducing the high-risk food items at this age group. Conventionally, one new food item is introduced over 3 days but this practice is not based on any scientific evidence yet can require a long duration to introduce multiple food items. Infants with early onset, moderate to severe atopic dermatitis have higher risk of developing food allergies, so they should not delay. The Australian Society of Clinical Immunology and Allergy (ASCIA) has developed a guidance for introduction of peanut containing food to infants at around 6 months old.(2) It starts with rubbing a small amount of smooth peanut butter or paste on the inside of infant's lip. If there is no allergy reaction few minutes later, ¼ teaspoon smooth peanut butter or paste can be introduced to the infant by mixing it into infant's usual diet or thinning with water. The infant is observed for another 30 minutes. If there is no allergic reaction, ½ teaspoon smooth peanut butter or paste can be given. If they develop allergy reactions, they should stop feeding the infant and seek medical advice immediately. For high-risk infants and parents are really concerned, they can also ask for medical advice to help them for early food introduction.

Q: There are new products containing single or multiple potentially allergic foods in the market, promoted as preventive aide in food allergy, what do you think about them?

A: There are different types of multi-allergen mixtures for infants for primary prevention of food allergy. They can help with early introduction of multiple food items within short period of time. Some food products are supported by scientific studies with low risk of food allergy. (3)

Q: What should parents be watching for if they choose to use these products?

A: For infants who are already known to have allergic reactions to the food components within a product, they should not take it. Different brands of the new multi-allergen mixtures have different amounts of food proteins. Some food proteins may not be stable after processing and packaging, which may affect the efficacy of food allergy prevention. If infants have adverse reactions to the food product, they should stop taking it and seek medical advice.

Q: What are the signs and symptoms during solid introduction that are red flags for seeing an allergist?

A: Acute food allergy reactions are mediated by IgE and the reactions happen quickly, usually within an hour, after introduction. Mild to moderate allergy reactions include urticaria and angioedema. Repeated vomiting,

persistent cough, shortness or wheezing, hoarseness, tongue swelling, pale looking and fainting are symptoms and signs of anaphylaxis which need immediate medical attention. Some food allergy reactions can have delay presentation like eczema flare, blood and mucous in stool, persistent diarrhoea and failure to thrive. If the above symptoms are present, an allergist assessment is recommended.

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Hong Kong Allergy Alliance Educational Symposium on Allergy in Hong Kong

Improving Allergy Care Standard through Transdisciplinary Collaboration

26 February 2023 (Sunday)

The Hong Kong Allergy Alliance Educational Symposium on Allergy in Hong Kong was successfully held on 26 February 2023 (Sunday) at The Hong Kong Academy of Medicine, Aberdeen Hong Kong.

The theme of the Symposium is "Improving Allergy Care Standard through Transdisciplinary Collaboration". The Symposium is an unparalleled opportunity championed by the highest academic medical institution of Hong Kong to bring aboard the Colleges in its Academy family to promote allergy education.

Overseas Meetings

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)

APAAACI 2023
23 - 26 October 2023 / Singapore (https://www.apaaaci2023.com/)

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 Scientific Forum 2023
24 June 2023

Hong Kong Allergy Convention 2023
7 - 8 October 2023