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Message from the Editor

Dr. Marco H.K. HO

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I would like to express my sincere gratitude to all the contributors who have played a pivotal role in making the Spring issue of the Hong Kong Institute of Allergy a resounding success. Your unwavering dedication and expertise have shone through, providing our readers with valuable insights and knowledge.

To Professor Chris Corrigan, HKIA we extend our gratitude for your enlightening article on Professor Lee Tak Hong's Inaugural Memorial Lecture which you have eloquently delivered in collaboration with the British Society for Allergy & Clinical Immunology at the 12^{th} Hong Kong Allergy Convention, $7 - 8^{th}$ October 2023. You have depicted lively Tak's incredible journey, pursuits and his life accomplishments in the international allergy and asthma research arena. Furthermore, your invaluable insights on the new understanding of blocking the Calcium-Sensing receptor and its implication for novel therapeutic target were a true delight for our readers.

Dr. Birgitta Wong has shared a short review on Cryotherapy as a treatment for Chronic Rhinitis, yet another exciting new treatment option to be explored in clinical practice. We are pleased to recognize Dr. James Hooi and Dr. Hugo Mak for their nominations for sponsorship to attend AAAAI 2024 one of the most prestigious informative international allergy conferences. Their dedication to furthering their knowledge and expertise in the field of allergy and immunology is commendable, and we wish them the best in post-conference sharing and future endeavors in clinical translation.

As we navigate the challenging economic downturn currently affecting Hong Kong, it is crucial to acknowledge the remarkable resilience and unity exhibited by our community. Despite the adversities brought about by the global pandemic, individuals and organizations have come together, demonstrating unwavering support and solidarity, and redefining the true essence of the holiday season.

Wishing you a peaceful and joyous Easter season regardless where you are heading to.

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

The Inaugural Professor Tak-Hong Lee Memorial Lecture In collaboration with the British Society for Allergy & Clinical Immunology

(Presented at the 12th Hong Kong Allergy Convention, 7 – 8th October 2023: Advances in Allergy Care)

Professor Chris J. CORRIGAN

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It was a great pleasure and honour to be invited by Professor Gary Wong, then President of the Hong Kong Institute of Allergy, Dr. Helen Chan and Dr. Roland Leung and the other members of the Organising Committee to present this lecture in honour of my friend and colleague Tak-Hong Lee, with whom I worked and collaborated for many years in London before he moved back to his native land and contributed so much to Allergy practice and training here in Hong Kong in the 11 years before recently departing this life. It was also a great pleasure to deliver this eulogy in the presence of Tak's son Adrian (Ady) Lee who was instrumental in the founding of the Lee Tak Hong Allergy Centre, founded recently in his honour.

Tak departed Hong Kong at the age of 10 and attended Marlborough College and Clare College, Cambridge, where he graduated with First Class Honours before training in Medicine and obtaining his MBBS at Guy's Hospital in London, where he later headed his own Department in which I joined him. After obtaining his medical degree, he worked with my former friend and colleague Professor Barry Kay as a Clinical lecturer in 1980 in the Department of Allergy & Clinical Immunology of the Cardiothoracic Institute at the Brompton Hospital. As a postgraduate, he worked with several other icons of excellence in asthma and allergy including dame Margaret Turner-Warwick, Jack Pepys, "Bill" Frankland and Jeffrey Drazen. In 1982 he was awarded a prestigious research scholarship to work with Dr. Frank Austen at Harvard University in his specialist research subject: the role of cysteinyl leukotrienes in asthma pathogenesis. He was appointed Clinical Senior Lecturer and Honorary Consultant at Guy's hospital in 1985, and the following year received the TV James Award from our British Medical Association for his asthma research. Tak was a bench-to-bedside, translational clinical scientist in asthma and allergy. He is well known for his research on leukotrienes and aspirin-exacerbated respiratory disease. Briefly, some of his key discoveries may be summarised as follows:

- 1. 1985: Functional studies of leukotrienes B, C, D and E derived from fish oil lipids. He discovered that ingestion of fish oil lipids by human subjects inhibits the production of LTB4 in favour of the less pro-inflammatory LTB5, suggesting that a diet rich in fish oil may have anti-inflammatory potential.¹
- 2. 1988: Inhalation of LTE4 enhances non-specific airways hyperresponsiveness in asthmatic subjects in vivo.²
- 3. 1989: Asthmatics, and in particular aspirin-sensitive asthmatics, display disproportionate airways hyperresponsiveness to LTE4 and compared with histamine and methacholine in vivo, a phenomenon attenuated by aspirin desensitisation, suggesting a n unique LTE4 recognition/signalling mechanism in asthmatic airways.³
- 4. 1991: Aspirin sensitive, as compared with tolerant asthmatics have elevated urinary LTE4 concentrations at baseline, further elevated following aspirin provocation, confirming dysregulation of the 5-lipoxygenase pathway in aspirin-sensitive patients.⁴
- 5. 1993: Eosinophils are recruited to, and degranulate in the airways of asthmatic volunteers following LTE4 inhalation, a novel pro-inflammatory activity of LTE4 relevant to asthma.⁵
- 6. 2002: Expression of the type 1 cysteinyl leukotriene receptor is down-regulated in the airways of aspirin-sensitive asthmatic patients following desensitisation.⁶

In 1988, aged 37, Tak was appointed Professor of Allergy and Allied Respiratory Disorders, a position funded by the Asthma Research Council (now Asthma and Lung UK): at this time, he was the youngest professor in the UK and was widely congratulated, not only by his parents and family but also his peers including Barry Kay and Stephen Holgate and Hugh Faulkner, then Director of the Asthma Research Council. It is salutatory to remember that Tak achieved all this despite having to cope with a life-threatening illness at this time, which required repeated surgery and engendered months of



suffering.

It is fair to say that the management of allergic disease in the UK was, at that time, in a sorry state. Allergic diseases were often branded as malingering; there were very few specialists and no systematised guidelines for the diagnosis and management of allergic diseases. Typically, in response to this, Tak had a vision of founding and Allergy Research Unit at Guy's, a goal which he attained in 1988. The Guy's Allergy Research Unit, funded by the Asthma research Council, commenced with an annual budget of £70K and comprised of Tak, a non-clinical Senior Lecturer (Mike Kemeny), 5 technicians, 7 junior researchers, 1 research nurse and 1 dietitian. In terms of clinical expertise, Tak was very ably assisted by Professor Maurice Lessof, Dr. Laurence Youlten and Dr. Bill Frankland: outstanding, eminent allergists who began to establish an evidence-based system of allergy diagnosis and management and helping administer the few therapeutic options available at that time, such as insect venom immunotherapy. Tak's fame began to blossom. In 1989 he was awarded, by HRH the Duchess of Gloucester, the title of BUPA Doctor of the Year. In 1996 Tak was elected President of the British Society for Allergy and Clinical Immunology and grasped the initiative of holding annual "think tanks" to facilitate translation of research in Allergy to development of clinical diagnostic and therapeutic services. This resulted in increased attendance and prestige at the annual BSACI meetings: at this time the Society had 467 members, and Tak's presidency saw the formation of clinical diagnostic standards, training programmes, the formation of specialist interest and young allergist groups and involvement of primary care physicians. To add to his accolades, Tak was named the Sunday Times Doctor of the Year and made a fellow of the UK Academy of Medical Sciences in 2000. In early 2000, as legend would have it while jointly making use of the gentlemen's lavatory during a social gathering, Tak and Barry Kay conceived the idea of joining the forces of the Medical Research Council, a major funder of medical research in the UK, Asthma UK, the national asthma organisation and two Colleges of the University of London (King's and Imperial Colleges) to form an alliance to foster broad based asthma and allergy research, from basic mechanisms to clinical practice, epidemiology, genomics and epigenomics and translational research. And so was born in 2005, with this immense and thoroughly novel initiative, the MRC and Asthma UK Centre for Allergic Mechanisms of Asthma. The success of this venture was bolstered by Asthma UK's research strategy to include allergic disease, and the extensive audit of allergy services in the UK carried out by the House of Lords Science and Technology Committee in 2007 (my first visit to the Houses of Parliament!). The Centre soon became populated with more than 30 clinicians and scientists across both Colleges, a thriving research programme and funding in excess of £100 million annually.

Despite these breath-taking advances, however, the clinical management of allergic diseases remained in its infancy in the UK. It was not until 1999 that the Department of Health and the Royal College of Physicians acknowledged Allergy as a separate speciality, and I personally undertook the task of assembling a training curriculum for Allergy, which in 2000 was endorsed by the Royal College of Physicians, the Postgraduate Medical Education and Training Board and the General Medical Council, establishing Allergy for the first time as a medical speciality and providing for National Training Numbers to fund the training of Specialist Allergy Registrars nationwide. I chaired the Specialist Advisory Committee on Allergy for the increasing benefit of all the patients out there suffering from allergic diseases. Nowadays at Guy's and St. Thomas's hospitals, in the shadow of Tak's work, we have extensive adult and paediatric Allergy services, a full portfolio of clinical Allergy services integrated with research, an extensive allergen immunotherapy service and flagship food and drug allergy services recognised by the World Allergy Organisation and GA2LEN as a Centre of Excellence. Curiously, because the speciality of Allergy was not recognised until 1999 in the UK Tak qualified as a chest physician and not an Allergist: I

remember that he had to fight though miles of red tape to be placed on the Allergy Specialist Register, doubtless fuelled by his desire to carry his amazing legacy back home to Hong Kong and establish Allergy as a speciality there too, a task in which he also admirably succeeded.

In 2012 Tak was appointed CBE by her majesty Queen Elizabeth II at Buckingham Palace in her Diamond Jubilee Year. One of my greatest privileges, having been invited to address the wonderful Hong Kong Allergists in Hong Kong last year, was to visit St. John's Cathedral where previously I had witnessed Tak's funeral service, then on a computer screen but now in the presence of his country, his family, his colleagues and his marvellous achievements. Rest in peace Tak.





Blocking the Calcium-Sensing receptor: the demise of asthma and COPD?

At this presentation I also presented a summary of the evidence collected by my colleagues showing that bronchial smooth muscle hyperresponsiveness, the cardinal clinical feature of asthma, is caused by over-expression of the Calcium-Sensing Receptor (CaSR) on airways smooth muscle cells. This receptor is composed of large extracellular domains comprised of two lobes, a cysteine-rich domain and a 7-transmembrane domain extending into the cellular cytoplasm. In a recent publication⁷ we showed that CaSR expression is increased on airways smooth muscle cells of patients with asthma and that this accounts for non-specific bronchial smooth muscle hyperresponsiveness in patients with asthma by elevation of the intracellular calcium. We also showed that a range of cationic proteins other than calcium, including the eosinophil basic proteins and cationic products of neutrophils such as spermidine can directly activate the receptor. In vitro, targeted deletion of the CaSR from human airways smooth muscle cells abrogated hyperresponsiveness. These data suggest that:

- The CaSR regulates free extracellular calcium in airways smooth muscle cells, which in turn regulates their contractile response to any contractile stimulus.
- Human asthmatics and animal surrogates of asthma show abnormal, elevated expression (and function?) of the CaSR, accounting for the phenomenon of bronchial hyperresponsiveness.
- Negative allosteric modulators of the CaSR, also termed calcilytics, which have already been developed for use in human patients for other possible therapeutic applications, and which can almost certainly be delivered topically to the airways using standard, asthma "inhaler" devices, have the propensity to abolish the phenomenon of bronchial hyperresponsiveness, eliminating symptoms and mortality and rendering bronchodilator therapy for human asthma redundant.

The fact that cationic proteins other than Ca2+ such as spermidine, polyamines from neutrophils and eosinophil cationic proteins can activate the CaSR provides the first functional link between airways inflammation and exacerbation of bronchoconstriction in asthma which has ever been described. These points are discussed in more detail in recent summaries.^{8,9,10}

We are currently also accumulating data suggesting that metallic cations, including calcium, in environmental particulates caused by atmospheric pollution can initiate airways inflammation by activating the CaSR expressed on airways epithelial cells. If so, regular topical calcilytic therapy, in addition to abolishing bronchial smooth muscle hyperresponsiveness in asthma, might also inhibit airways inflammation, remodelling and irreversible obstruction seen in patients with COPD and some with asthma.

We are very excited about the possibility of performing "First in human" studies on asthmatics, where it should be straightforward to test our predicted hypothesis that topical inhalation of a suitable calcilytic abolishes bronchial hyperresponsiveness in patients with asthma. We would be very interested in collaborating with any colleagues from the pharmaceutical or related industries to achieve this goal.

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Cryotherapy for Treatment of Chronic Rhinitis

Dr. Birgitta Y.H. WONG

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Chronic rhinitis is a common disease affecting around 320 million people worldwide.¹ It is subdivided into allergic and non-allergic rhinitis. Medical treatment is the firstline therapy including corticosteroids, antihistamines, nasal spray and irrigation. Immunotherapy is an option for selected patients. Surgical treatment is reserved for refractory cases and seldomly performed. Vidian neurectomy has been used to disrupt parasympathetic innervation of the nasal mucosa. However, complication dry eye from simultaneous disruption of of parasympathetic innervation to the lacrimal gland can occur and the surgery has to be done under general anaesthesia. Later the use of posterior nasal nerve was advocated to focally disrupt onlv the nasal parasympathetic innervation distal to the parasympathetic fibres for lacrimal innervation. Recently, cryotherapy was used to ablate the posterior nasal nerve reduce nasal discharge and obstruction.^{1,2,3} to Cryotherapy is to apply nitrous oxide cryogen through a hand-held cryoprobe under nasoendoscopy guidance at the posterior nasal nerve around the site of the sphenopalatine foramen.³ The procedure can be done under local anaesthesia with a 30 second freeze and 60 second thaw cycle on each side of the nose. The technique offers ablation of the soft tissue and nerve with predictable depth of penetration, preserving the vascular strip to the region and minimizes the risk of necrosis.²

There are increasing number of papers on this technique. One paper was published in 2023 on a systemic review of 'Cryoablation for the treatment of chronic rhinitis'.¹ Eight articles were included, one was an RCT and 7 were singlearm cohort studies. A total of 472 patients were evaluated across all studies. The data showed that the Total Nasal Symptom Score (TNSS) for assessing rhinorrhoea, nasal congestion, nasal itchiness and sneezing showed a statistically significant improvement after one month and 3 months. The most common adverse effect reported was post-procedural pain or discomfort, ranging from 74% in some patients. Other complications included headache, palate numbness, epistaxis and nasal swelling.¹ However this systematic review has several limitations such as no information on the long-term effect of cryotherapy of posterior nasal nerve on reduction of nasal symptoms. Besides, the studies did not delineate allergic and non-allergic rhinitis which may have different response to ablation of parasympathetic stimulation. Additionally, five of the eight studies are from the same cryoprobe device company, the impact on the overall study findings are unclear.

There is another paper published on 'Cryotherapy for treatment of chronic rhinitis: 3-month outcomes of a randomized, sham-controlled trial.² This study is a multicenter, randomized sham-controlled, patient-blinded trial. The purpose is to test whether cryotherapy is better than sham procedure for reducing rhinitis symptoms. 133 patients with rhinitis duration more than 2 years were recruited with 68 active and 65 sham. For the active group, patients received cryotherapy ablation of the posterior nasal nerve under local anaesthesia. For the sham surgery group, the cryoprobe was also placed in the nasal cavity posterior middle meatus with the sound of gas release. Total nasal symptom scores and Quality of Life Questionnaire (RQLQ) were evaluated. Results showed total nasal symptom scores had significant greater improvement for rhinorrhoea and nasal congestion in the active arm compared to sham arm. Nasal itchiness and sneezing were not significantly different between the treatment arms. For RQLQ, the active arm showed significantly greater improvement over the sham arm at 90-day visit. The commonest adverse effects were pain and discomfort at the cryotherapy site intranasally in 26 patients.² This is the first randomized prospective trial of cryotherapy as treatment for chronic rhinitis and the results support the use as a viable option without serious complication and the procedure can be done in clinic setting. The weakness of this study is the lack of long-term results and there is no data on the duration of effect as this moment yet.

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American Academy of Allergy Asthma & Immunology Annual Meeting 2024 23 – 26 February 2024

Dr. James K.Y. HOOI

MBChB (CUHK), MRCP(UK) Higher Physician Trainee in Immunology and Allergy Department of Medicine, Queen Mary Hospital, Hong Kong

The 2024 American Academy of Allergy Asthma & Immunology Annual Meeting (AAAAI) was hosted this year in Washington D.C., and it was my privilege to be able to attend this conference with the support provided by CSL Behring. The AAAAI 2024 was a week-long conference that boasted an impressive program, including a wide variety of content-rich sessions covering the latest in allergy/immunology, all built around the theme of Collaboration, Discovery, Innovation. The meeting had thousands of attendees from a community of allergists/immunologists and scientists that that had all gathered to learn from the top experts in the field, and as a trainee in Immunology and Allergy, the opportunity to attend this conference was truly an unforgettable experience.



Firstly, the conference provided a variety of practical workshops to teach the up-and-coming skills required in our field, for example, a practicum on incorporating oral immunotherapy in the clinic or a introductory rhinolaryngoscopy course, which I had attended. The session provided a comprehensive review of the anatomy of the ear, nose and throat, followed by demonstrating the utility of having performing your own rhinolaryngoscopy in clinic. This session not only guided me on how to use a laryngoscope, but also, that as internists, we can still be very hands-on with our patients, and visualize directly the effect of our medication on the body.

The conference program featured symposiums on a comprehensive array of topics, addressing pressing challenges and emerging areas of interest within immunology and allergy. The eminent experts from around the globe, combined with the interactive nature of the workshops, fostered an environment conducive to intellectual exchange and learning. One of the most memorable lectures was on the groundbreaking OUtMATCH study on the newly FDA approve for use of Omalizumab in the treatment of food allergies, which was a double-blind, randomized, placebo-controlled trial on patients who had proven allergies to certain foods. The study showed that treatment with omalizumab was superior to placebo in increasing the reaction threshold for common food allergens, the implications of which may lead to the reduction of life-threatening reactions for those with serious food allergies, and potentially could changing the way allergists treat food allergy.

Beyond the presentations, the conference fostered networking and collaboration amongst immunologist/allergists from all over the world. The vibrant atmosphere encouraged interactions between healthcare professionals, researchers, and industry representatives, facilitating the exchange of ideas and the formation of new connections, overall further strengthening the collective pursuit of advancements in immunology and allergy research and patient care. The event also brought hundreds of different scientific posters that covered innovations in different areas of the specialty, which reminded me the vast scope of our practice and potential areas of improvement in local practice.

AAAAI 2024 served as an extraordinary platform cutting-edge research and innovatory education in the field of Immunology and Allergy, delivered by some of the best in the specialty. Through this conference, I have done my best to

Meeting Highlights



absorb the latest insights, engage in productive discussions and hopefully enhanced my understanding of the rapidly evolving field. I would, firstly, like to thank my supervisor Dr Philip Li for nominating me to attend this indelible event, and also express my deepest gratitude to CSL Behring for their sponsorship. The insights gained and the connections made during this conference will undoubtedly have a lasting impact on my professional growth and, more importantly, on the well-being of the patients I see in the future.



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A Glimpse into the Future of Allergy Care and Research: My Experience at the AAAAI 2024 Annual Meeting 23 – 26 February 2024

Dr. Hugo W.F. MAK

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The American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Meeting was one of the largest and most prestigious events in the field of allergy. It gathers experts from across the globe and features the latest advances in the research and clinical care of various allergic and immunological diseases. Generously supported by the Hong Kong Institute of Allergy (HKIA), I had the precious opportunity to attend the AAAAI 2024 Annual Meeting, which was held in Washington DC from Feb 23 to 26 with the theme of "Collaboration, Diversity, Innovation".

During this event, I presented two of my recent projects, respectively regarding drug allergy and chronic spontaneous urticaria (CSU). The first project I presented was about the development and validation of the Short Drug Hypersensitivity Quality of Life Questionnaire (DrHy-Q6), which was recently published in the Journal of Allergy and Clinical Immunology: In Practice.¹ In this study, we used item response theory, a modern statistical school for psychometric analysis, to select the best-performing items from the original 15-item questionnaire (validated and available in Chinese² and constructed an abbreviated version with superior psychometric properties and scoring algorithms. This optimised 6-item version was concise, precise and easy to use, which we recommend to be used in routine clinical practice for patient-centred care.



The second study I presented shed light on health disparity, particularly pharmacoequity in CSU, as exemplified by the disparities in access to CSU biologics in Hong Kong.³ Our group found that patients eligible for drug reimbursement were more likely to receive biologics (omalizumab) for their CSU, ultimately leading to better disease outcomes than those who could not reimburse their therapies. Our study showed how differential patterns of management, primarily due to non-clinical factors, could translate into inferior patient outcomes, calling for efforts to promote guideline- and evidence-based care in CSU. This study was recently published in the Journal of Allergy and Clinical Immunology: Global.

At the whole meeting, one of the most notable studies was the OUTMATCH study presented in a late-breaking symposium on the last day of the conference. The OUTMATCH study was a randomised controlled trial investigating the efficacy of omalizumab for multiple food allergies.⁴ Published in the New England Journal of Medicine on the day of presentation, the study demonstrated that omalizumab could reduce allergic reactions and increase the reaction threshold for a number of common food allergens (peanut, cashew, milk, and egg) among food-allergic patients. Undoubtedly, this is a significant breakthrough that will lead to a paradigm shift in food allergy care.⁵ Beyond efficacy, echoing the aforementioned studies, the impact of the expanded indication of omalizumab on equity and patients' QoL in food allergy will also be worth investigating and warrant future studies.

As of interest to many, artificial intelligence (AI) and machine learning (ML) had a prominent place at the meeting as well, with multiple projects highlighting their multifaceted potential in allergy care and research. There were scholars developing ML models to respectively predict the outcomes of peanut oral food challenges, as well as penicillin drug provocation tests, based on data from large, prospective cohorts. Some other innovative ideas included evaluating the potential of generative AI, such as ChatGPT, in providing healthcare information for patients and medical professionals compared to patient education materials and clinical guidelines for anaphylaxis, drug allergy and allergic rhinitis. Another group used natural language processing to perform automated data extraction from unstructured clinical notes and referral letters, aiming to facilitate drug allergy care and research. While many of these studies were still in their early



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stages, I really look forward to incorporating these advancements into my research and practice to improve patient outcomes.

Outside the conference, I also had the chance to explore the beautiful city of Washington DC during my free time. I visited the National Museum of Natural History and the iconic Lincoln Memorial, both of which offered enriching experiences and a chance to appreciate the rich history and culture of the city. Overall, my experience at the AAAAI 2024 Annual Meeting was both educational and inspiring, and I am excited about the future of allergy care and research.

Last but not least, I would like to express my deepest gratitude to the HKIA for their generosity, which made my attendance at the AAAAI 2024 Annual Meeting possible. The HKIA's commitment to fostering the growth and development of young allergists and researchers in Hong Kong is truly commendable. Their support has not only enriched my knowledge and understanding of the latest advancements in allergy care and research but has also provided me with an invaluable opportunity to network with experts and professionals in the field. I am truly grateful for the HKIA's unwavering dedication to improving patient care and outcomes in the realm of allergy and immunology.



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Hong Kong Chronic Spontaneous Urticaria (CSU) Expert Meeting 26 March 2024

The Hong Kong Chronic Spontaneous Urticaria Expert Meeting was successfully held on 26 March 2024 at Sheraton Hong Kong Hotel & Towers.

The objective of the meeting was to provide a platform for clinical experts to discuss the up-to-date scientific information and clinical practice on various important topics including local guideline, global guideline, on-going clinical trials, and data on emerging novel therapies in the management of urticaria.

We are honored to have Professor Marcus Maurer (Professor of Dermatology and Allergy and Executive Director of the Institute of Allergology at the Charité – Universitätsmedizin Berlin), Dr. Ricardo Coelho (Consultant, Department Head of Dermatology, Conde S. Januário Hospital, Macau, and Dr. Philip Li to deliver the lectures at the meeting. The meeting was well attended by 25 experts, and they had active discussions on the topic.

An educational leaflet of Hong Kong-Macau Severe Hives and Angioedema Referral Pathway was developed by Dr. Philip Li for distribution at the meeting (Appendix A).











Hong Kong-Macau Severe Hives and Angioedema Referral Pathway (Hong Kong-Macau SHARP)

Philip H Li, Elaine Y L Au, Si-Leong Cheong , Ling Chung, Ka I Fan, Marco H K Ho, Agnes S Y Leung, Martin M H Chung , Jane C Y Wong, Ricardo Coelho Front Allergy. 2023 Dec 6:4:1290021. doi: 10.3389/falgy.2023.1290021.

Full Version of Article:

(Appendix A)



- 1. Urticaria is characterized by wheals/hives, angioedema (AE), or both
- Urticaria classified as: Acute (≤6 weeks) or Chronic (>6 weeks) AND Spontaneous or Inducible
- 3. "Severe CSU" = UAS7 >27, or equivalent

Classifications & Definitions

- 1. No routine investigations for CSU except when immediate-type allergy suspected
- 2. Regularly assess CSU with **patient reported outcome measures**, e.g. UAS7
- 3. Classification of AE by etiology: Mast cell- or BK-mediated

Diagnosis

- Diagnose CSU clinically and blood tests not usually necessary, unless other diagnoses suspected
- 5. No routine allergy tests and skin biopsies for CSU
- 6. Exclude ACEI-AE first in all patients with AE
- 7. C1-INH deficiency considered in BK-mediated AE (after ACEI-AE excluded)
- 8. Initial screening for low C4 levels in BK-mediated AE
- 1. Treatment aim = complete symptom control and normalization of quality of life
- 2. Regular 2nd generation H1 antihistamines for CSU
- 3. Increase 2nd generation H1 antihistamines **up to 4x if unresponsive** to standard doses, before other treatments
- 4. **Do not combine anti-histamines** (especially 1st generation) at same time for urticaria
- 5. No long-term use of steroids in treatment of urticaria
- 6. No ACEI in patients with a history of spontaneous AE
- 7. No antihistamines, steroids, or adrenaline for confirmed BK-mediated AE
- 8. Referral to dermatology or I&A center for severe CSU not responding to 4x dosing of 2nd generation H1 antihistamines
- 9. Omalizumab for severe CSU not responding to 4x dosing of 2nd generation H1 antihistamines
- 10. Cyclosporin for severe CSU when omalizumab is unavailable/contraindicated
- 11. Referral to dermatology or I&A specialist for suspected BK-mediated AE, when ACEI-AE excluded
- 12. No non-HAE-specific medications for treatment and prophylaxis of HAE

(ACEI = Angiotensin Converting Enzyme Inhibitor, AE = Angioedema, BK = Bradykinin, C1-INH= C1 Esterase Inhibitor, C4 = Complement 4, CSU = Chronic Spontaneous Urticaria, HAE = Hereditary Angioedema, I&A = Immunology & Allergy, UAS7 = Weekly Urticaria Activity Score)

Management & Referral





(Appendix A)

Hong Kong-Macau Severe Hives and Angioedema Referral Pathway (Hong Kong-Macau SHARP)

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Overseas Meetings

EAACI Congress 2024 (European Academy of Allergy and Clinical Immunology Congress 2024) 31 May - 3 June 2024 / Valencia, Spain (<u>https://eaaci.org/events_congress/eaaci-congress-2024/</u>)

ERS 2024 (European Respiratory Society Congress 2024)

7 - 11 September 2024 / Vienna, Austria (https://www.ersnet.org/congress-and-events/congress/)

CHEST 2024 (The American College of Chest Physicians Annual Meeting 2024)

6 - 9 October 2024 / Boston, MA (https://www.chestnet.org/Learning-and-Events/Events/CHEST-Annual-Meeting)

ACAAI 2024 (American College of Allergy Asthma and Immunology Annual Scientific Meeting 2024) 24 - 28 October 2024 / Boston, MA (<u>https://annualmeeting.acaai.org/</u>)

Local Meeting

28th Congress of the Asian Pacific Society of Respirology (APSR 2024)

7 - 10 November 2024, Hong Kong (https://www.apsr2024.hk/)