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## Message from the Editor

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Again, the editorial team as always is grateful to all the contributors. We are happy to conjecture a wonderful 5 course meal to provide a structured and well-balanced “reading” experience that allows audience to savor a variety of “flavors and ingredients” for this Fall issue.

Dr. David C. M. YEUNG has given an aromatic appetizer. Disorders of the sense of smell, known as olfactory disorders, can significantly impact quality of life. Dr Yeung’s concise narrative on intranasal and extranasal components becomes a true delight.

Dr. Ka-wai KAM and colleagues have offered a mixed freshy “salad” which contrasted the latest European Expert Consensus with the Asia Expert Working Group (MOVIA) consensus in the management of Vernal Keratoconjunctivitis (VKC) and how it can be applied to the treatment of VKC in Hong Kong. There are similarities and differences. The intriguing part is that Asian Consensus devoid allergen-specific immunotherapy whilst European one advises as an adjunct for severe disease. I munch quite a while to aid my digestion of take-home messages- one of them being Asia perhaps lacks a service infrastructure to cater for the demand or genuine need of immunotherapy.

Considering the recent tragic events of Hong Kong citizens succumbed to insect-stung anaphylaxis, Dr. Gilbert T CHUA has given us a stingy stimulating entrée by overviewing on types of insects associated with venom allergies, diagnostic approaches, emergency treatment, and venom immunotherapy. Hope such incidents serve as a wakeup call to all of us. The awareness remains low. HK citizen deserves better anaphylaxis management.

In acknowledging HKIA’s research grant support, Dr. O.M. CHAN has summarized her novel original work about different cooking effects on allergenicity of Cashew nut which sheds light towards the establishment of a “safe” level of allergenicity necessary for successful oral immunotherapy. This nutty main course is worth the good money from HKIA. We look forward to more products of this good quality.

Dr. Sonal HATTANGDI-HARIDAS has contributed a succinct article on the inflammatory correlation between ADHD and Atopic Diseases, a contentious topic of research of gaining new insights. Much like chocolate lava cake going well with coffee- expecting for another good time together.

Don’t forget “old wine and friends improve with age” I would like to serve you with an inspirational “old wine” along with the 5-course meal. I have interviewed one of the founders and a Past President of HKIA- Professor Christopher Lai. His wisdom gives budding clinical leaders and physician-scientists a lot of food/tannins for thought. Enjoy!

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

## Interview with the Founding Council Member – Professor Christopher Lai

### Research is the Base of Knowledge

*"Allergy and asthma research contributes to the existing body of knowledge by uncovering new insights, validating existing theories, or challenging prevailing assumptions"* – Professor Christopher Lai.

It is my pleasure to have an Interview with Professor Christopher Lai on 21 September 2024 at the Hong Kong Jockey Club Happy Valley Clubhouse. Professor Lai is the Founding Council Member of the Institute. Together with the late Dr. Avery Chan, Dr. Helen Chan, Dr. Ka-ho Chan, Dr. Jane Chan, Dr. John Leung, Professor William Wei, the late Dr. William Yip, Dr. Donald Yu, Dr. Hip-cho Yu and Dr. Patrick Yuen, he set up the Institute in 1996.

From the 1990s, while doctoring in the Chinese University of Hong Kong, Professor Lai conducted many researches and published over 150 papers in peer-reviewed journals. Professor Lai was a member of the steering committee of the world-renowned ISSAC study which not only documented the breadth and depth of the global prevalence of Allergic Diseases but also raised the possible risk factors for the development of these diseases and increased awareness of Allergy among the public and professionals worldwide.

Professor Lai was awarded the "HKIA Outstanding Contributions to Clinical Allergy Award 2018" and the "Lifetime Distinguished Service to HKIA" in 2021. These are the highest honours that the Hong Kong Institute of Allergy (HKIA) can bestow. It recognises the distinction of an individual not only for the achievements in the clinical researches, but also for the contributions to the Institute, and to the growth of the discipline of allergy in the HK community.



#### Question 1: Could you please tell us your most memorable research experience?

As one of the pioneers in the research in Allergy in Hong Kong, I cannot think of another more suitable person than Professor Christopher Lai to talk on this topic. Professor Lai had started many research projects with the Chinese University of Hong Kong when he returned to Hong Kong in 1998.

When I asked Professor Lai for his most memorable research experience, his mind flied back to the time when he spent 6 years in the UK to pursue training in clinical respiratory medicine in Scotland from 1983 to 1986 and another 3 years in full-time research in the pathogenetic mechanisms of asthma in Southampton, under the mentorship of Professor Sir Stephen Holgate. During this period of research training, he also participated in the outpatient care of patients with various allergic diseases.

Professor Lai emphasized the importance of integrating clinical practice with research, noting that his involvement in the Asthma field was particularly memorable. This study aimed to explore the epidemiology of asthma across different demographics, utilizing validated questionnaires to assess experiences and symptoms of patients. The collaborative environment fostered by leading researchers in the UK not only enhanced his research acumen, but also established a foundation for his future contributions to allergy research in Hong Kong.

#### Question 2: Dare to Challenge the Authority and Seek the Truth?

Research integrity was of paramount importance. With the evolving world and advancing technologies, some past research endeavors were debunked. Professor Lai stressed the importance of renowned research experts being receptive to challenges. Researchers should engage in rational thinking, pose questions upon encountering unique epidemiological phenomena, and strive for truth-seeking. This philosophy stood as the cornerstone of research

*"Researchers should often dare to step out of his or her comfort zone. Don't just focus on the short-term monetary gain"*

Professor Lai was still sitting on committees vetting for research proposals. He commented that validation of questionnaires was missing in Hong Kong. It might lead to bias on the research results at the end. An example was the International Study of Asthma and Allergies in Childhood (ISAAC Study). Its questionnaire was translated into 100 languages and back translated to make sure the meaning of the questions was the same in different languages. It would ensure more accurate information and data from different geographic areas were collected. It would be a good lesson to draw upon.

### **Question 3: How does Hong Kong compare with the rest of the world in allergy service training and research?**

Professor Lai articulated that Hong Kong has made significant strides in allergy service, training and research, positioning itself as a leader in the Asia-Pacific region. He highlighted the establishment of comprehensive training programmes that aligned with international standards, which had been instrumental in cultivating a new generation of allergists.

Professor Lai noted that while Hong Kong's allergy service was robust, it remained a gap in public awareness and understanding of allergic conditions compared to western countries. He referenced the needs for more extensive researches into food allergies, particularly considering the increasing prevalence of conditions such as food-induced anaphylaxis. Professor Lai pointed out that collaborations with global research network was essential for advancing local practices, and ensuring that Hong Kong remained at the forefront of allergy research.

### **Question 4: What is your view on the development of the healthcare landscape?**

Professor Lai expressed a forward-looking perspective on the evolving healthcare landscape in Hong Kong, emphasizing the critical role of research in shaping effective healthcare policies and practices. He underscored the necessity of evidence-based medicine, particularly in the context of allergy management, where scientific validation of treatment protocols is of paramount importance.

*"As you move outside of your comfort zone, what was once the unknown and frightening becomes your new normal and new knowledge"*

Professor Lai discussed the importance of integrating new technologies and methodologies, such as immunotherapy and desensitization techniques, into clinical practice. He advocated for a multidisciplinary approach in the development of the healthcare service that included collaboration among allergists, general practitioners and researchers to enhance the treatment outcomes.

Furthermore, the importance of public education initiatives was stressed to raise the awareness about allergies and their management, which Professor Lai believed, would lead to the improved health outcomes and quality of life for patients.



Dinner with our Patron, Dr. Ko Wing-man  
(10 July 2015)



Photo taken at  
Annual Scientific Meeting 2024  
(6 October 2024)



Enjoying golf with Late Professor Tak Lee  
and friends



Work life balance: meeting friends at the golf  
course every Wednesday



Precious time with Mrs. Chermey Lai and  
grandchildren at the Hong Kong Disneyland

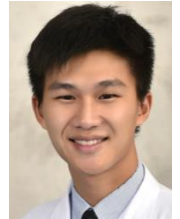


Beautiful grand children: (from left to right)  
Hugo, Lena, Heston and Jenson

## Smell and Rhinological Diseases

**Dr. David C.M. YEUNG**

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Smell, or olfaction, is one of the five primary senses that plays a crucial role in human experience, impacting daily life, emotional well-being, and safety. It is integral to the perception of flavor, influencing taste and enhancing the enjoyment of food. Beyond mere pleasure, the sense of smell serves essential functions, such as detecting hazards and contributing to social interactions, identity, and attraction. Furthermore, olfactory cues trigger memories and emotions, highlighting the profound connection between smell and psychology.

Disorders of the sense of smell, known as olfactory disorders, can significantly impact quality of life. Conditions such as hyposmia (reduced ability to smell) and anosmia (complete loss of smell) can arise from various causes. These conditions not only diminish sensory experience but can also lead to nutritional deficiencies, as individuals may lose interest in food or be unable to detect spoiled items, resulting in food toxicities for themselves or those they care for. In a sample of 704 patients with smell and taste disorders, the incidence of hazardous events was related to the degree of smell dysfunction with up to 39.3% for patient with anosmia, and 22 - 32% for hyposmia<sup>1</sup>. Additionally, olfactory disorders can contribute to emotional and psychological issues, such as depression and anxiety<sup>2</sup>, due to their influence on social interactions and overall quality of life<sup>3</sup>.

The olfactory pathway can be delineated into two primary components: intranasal and extranasal. The intranasal component initiates with the detection of odorant molecules by olfactory receptor neurons located in the olfactory epithelium within the nasal cavity, particularly in the olfactory cleft and the superior turbinate. Anatomical variations that influence laminar airflow and the delivery of odorant molecules, as well as any processes that impact the integrity of the olfactory mucosa, can result in olfactory disorders. These

conditions can arise from a variety of rhinological diseases.

Up to 44% of children with allergic rhinitis exhibit smell dysfunction. Among individuals with chronic rhinosinusitis, a systematic review indicates that the prevalence of smell dysfunction can be as high as 30%. Furthermore, acute anosmia or ageusia has been reported in 15.3% of patients during the early stages of COVID-19, with a prevalence of 15.7% observed in those with asymptomatic to mild disease severity. Other etiologies include both infectious conditions and the presence of benign or malignant tumors.

Differentiating these disorders necessitates a comprehensive clinical history, accompanied by an otolaryngological examination, which may include rhinoscopy or tissue biopsies for pathological diagnoses. Additionally, olfactory assessments through subjective smell loss questionnaires and quality of life impact assessments, as well as objective smell tests such as the Sniffin' Sticks test, University of Pennsylvania Smell Identification Test (UPSIT), and Top International Biotech Smell Identification Test (TIBSIT), are essential for characterizing and quantifying the degree of olfactory loss.

The conversion of detected odor molecules into neuronal signals that travel through the skull base to the olfactory bulb marks the start of the extranasal component. This information is processed and transmitted to several brain regions, including the piriform cortex, amygdala, and hippocampus<sup>4</sup>. Neurological diseases associated with smell loss include Parkinson's disease, Alzheimer's disease, and head trauma<sup>5</sup>.

Achieving optimal smell function in rhinological diseases is challenging, as there are still many unknowns regarding both the sensory and neurocognitive components.

Therefore, optimally treating a condition may not necessarily lead to ideal smell outcomes. In terms of smell recovery in rhinological diseases, one should aim to rehabilitate the intranasal condition, whether medically or surgically, while also promoting neuroplasticity within the olfactory pathway<sup>6</sup>.

A smell unit that offers subspecialty care for rhinological conditions, smell training<sup>7</sup>, and adequate counseling—along with follow-up reviews facilitated by a smell nurse—can all contribute to successful smell recovery. In cases requiring surgery, meticulous surgical planning to preserve olfactory-related structures while maximizing surgical results<sup>8</sup>, combined with pre- and postoperative medical therapy, will also enhance smell recovery.

The sense of smell is an essential component of human experience, influencing nutrition, safety, and emotional well-being. Recognizing the role of smell as a functional treatment outcome in both medical and surgical interventions marks the beginning of smell recovery. This process involves proper functional assessment, endoscopic examination, follow-up care, counseling, and, if available, involvement from subspecialty personnel.

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## Diagnosis and Management of Vernal Keratoconjunctivitis in Asia: Consensus and Challenges

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### Introduction to Vernal Keratoconjunctivitis

Vernal Keratoconjunctivitis (VKC) is a type of chronic, allergic inflammation of the ocular surface that is characterised by intense ocular itching, photophobia, redness, swelling and discharge. Children and young adults, especially males are primarily affected by VKC, which can significantly impair their quality of life and daily activities (1). This article will compare the latest European Expert Consensus with the Asia Expert Working Group (MOVIA) consensus in the management of VKC and how it can be applied to the treatment of VKC in Hong Kong.

### Prevalence of VKC

The prevalence rate of VKC varies globally across different ethnic groups and regions, and is influenced by climate and environmental factors. It is more common in tropical areas and temperate zones of the Mediterranean areas, Central, West and South Africa, the Middle East, Japan, and the Indian subcontinent. However, cases have also been reported in almost every part of the world. The prevalence of VKC ranges from 1.2

to 10.6 cases per 10,000 population in Europe (2), and between 2-37% in Africa (3). In Asia, comprehensive data on prevalence is limited. For instance, only Japan reported a prevalence rate of 1.2%, but the actual figure is likely higher due to mild, self-limiting cases that often go unreported. VKC also frequently resolves around puberty, which may further contribute to the underestimation (4).

### Diagnostic Approaches

In Europe, primary healthcare physicians and general ophthalmologists prioritise identifying key symptoms such as intense itching, photophobia, redness, increased tearing, and blurred vision. The slit-lamp examination is used to identify hallmark signs such as giant cobblestone-like papillae, Horner-Trantas dots and shield ulcers. Eversion of eyelids should also be done to evaluate the palpebral conjunctiva for signs of inflammation. The presence of these signs accompanied by severe or persistent symptoms (following 1-2 weeks of conventional treatment) should prompt a referral to specialists as early intervention may prevent complications and improve treatment outcomes (5).

In Asia, particularly in India and China, perilimbal hyperpigmentation was observed as a sign of VKC. These fine golden brown spots in the perilimbal bulbar conjunctiva are thought to be a by-product of the interactions between melanocytes, mast cells and the immune mechanisms behind VKC. Further research is needed to delineate its diagnostic or prognostic value. The experts in the Asian consensus also reported that the Bonini scale was the most frequently used grading system across Asia in determining the severity of VKC. The scale is separated into 6 different stages, ranging from quiescent (grade 0) to evolution (grade 5), with grade 4 being the most severe. The Bonini scale assesses both the symptoms and signs, with the aid of standard photographs (6).

### Sight-Threatening Complications

In advanced stages, VKC can lead to serious corneal complications and potentially result in permanent vision loss. Persistent and intense ocular surface inflammation is believed to be the major culprit to these serious outcomes. Initially, patients may develop superficial punctate keratitis, which are fine cracks on the surface of the cornea, and they occur when chronic inflammation damages the corneal epithelium. This can further progress into epithelial defects and the development of shield ulcers. These complications reduce the cornea's transparency, causing blurred vision and photophobia. Even after a shield ulcer heals, scarring beneath the surface can occur. This scarring disrupts how the cornea refracts light, leading to significant visual impairment and astigmatism. Additionally, some studies propose a link between ongoing inflammation in VKC and keratoconus, which is a progressive deformation of the cornea, resulting in severe astigmatism and vision loss (7).

### The Ladder Approach to Medical Treatment

Recently, both Asia and Europe have come up with a revised treatment approach that reflects advances in technology, with Asia placing additional emphasis on practical considerations related to healthcare access. The current approach in Asia begins with exposure avoidance and the use of ocular lubricants and cold compress to alleviate mild symptoms. Dual-acting agents with both antihistamines and mast cell stabilisers are preferred over monotherapy as they are well tolerated, have a longer duration of action and higher potency with fewer side effects. Topical calcineurin inhibitors, such as cyclosporine A or tacrolimus are introduced earlier, especially in the more recent Asian report, than short-

pulse corticosteroids. These agents help to reduce ocular surface inflammation by inhibiting T-helper 2 cell proliferation and Interleukin 2 production. In contrast, short-pulse topical corticosteroids should be used cautiously as add-on or rescue therapy when symptoms are severe, in order to minimise the risk of raised intraocular pressure/glaucoma, and/or cataracts. Thus a softer topical corticosteroid such as loteprednol is preferred among the experts. If an allergy is critically identified, systemic treatments such as immunomodulators or anti-IgE biologics are considered after referring to an allergist. Oral corticosteroids or corticosteroid injections can also be considered for recalcitrant cases, with surgeries used as a last resort if medical therapy is insufficient. Last but not least, vasoconstrictors and NSAIDs are not recommended as they do not target the specific inflammatory mechanisms associated with VKC in the Asian consensus (5).

The European consensus also uses similar non-pharmacological conservative measures for mild cases, including allergen avoidance and symptomatic relief with cold compresses and ocular lubricants. For moderate and severe VKC, topical dual acting agents are also recommended over monotherapy, followed by short pulses of corticosteroids, either alone or in combination with topical calcineurin inhibitors, while vasoconstrictors and NSAIDs are also not recommended. However, there is a stronger emphasis on using corticosteroid sparingly, and frequent specialist consultations should be made to ensure corticosteroids are only used under strict supervision (6). However, this is less attainable in Asia, due to the less robust healthcare infrastructure in some parts and regional disparities in healthcare access.

### Surgical Interventions

Both the European and Asian guidelines recommend ophthalmologist consultation for VKC patients who may benefit from surgical interventions. Some of the suggested indications from the Asian consensus include persistent cobblestone papillae, shield ulcers, corneal plaques, limbal stem cell deficiency, and other ocular surface conditions unresponsive to medical treatment. Procedures such as papillectomy, corneal plaque debridement, and amniotic membrane transplantation have been shown to facilitate re-epithelialization of the ocular surface and reduce complications associated with medical therapy. However, cryotherapy and excision of giant papillae should be avoided as they do not treat the underlying disease and may induce unnecessary scarring (8). In refractory VKC with extensive limbal damage,

conjunctivalization can occur and severely reduce vision. Limbal stem cell replacement by allogeneic tissues and systemic immunosuppression were shown to achieve good clinical outcomes (9, 10).

### Conclusions

The Hong Kong medical community could benefit from integrating elements from both consensus guidelines for managing VKC. Increasing awareness of VKC among primary care physicians is essential for distinguishing it from milder forms of allergic conjunctivitis. Techniques such as everting the upper eyelids to examine the palpebral conjunctiva, along with the use of standard photographs, can aid family physicians in identifying potential VKC cases. Accurate detection is vital, as the quality of referrals significantly impacts specialist care within our public healthcare system. The Bonini scale can help general practitioners and paediatricians assess VKC severity and refer severe cases to ophthalmologists. When considering treatment, the use of topical calcineurin inhibitors must be balanced against costs, particularly in the public sector. Both consensus documents lack clear guidance on when to taper or discontinue these medications, raising concerns about long-term expenses.

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Table 1. Comparison between the European and Asian Expert Consensus on the Management of Vernal Keratoconjunctivitis

Severity	Asia	Europe
Mild	- Exposure avoidance	- Exposure avoidance
	- Ocular lubricants and cold compresses	- Ocular lubricants/artificial tears and cold compresses
	- Dual-acting agents (Antihistamines and mast cell stabilisers) preferred over monotherapy	- Dual-acting agents (Antihistamines and mast cell stabilisers) preferred over monotherapy
Moderate	- <b>Topical calcineurin inhibitors</b> like CsA is introduced earlier than corticosteroids	- <b>Short pulse corticosteroids</b> alone, or as add-on to topical CsA, as rescue therapy
	- Short-pulse topical corticosteroids as add-on or rescue therapy	
Moderate to Severe	- Systemic treatment (immunomodulators or anti IgE biologics)	- Topical immunomodulators considered for moderate - to severe or persistent VKC to provide long-term control
		- High frequency corticosteroids or oral corticosteroids (short-pulses) for persistent corneal complications or non-response to prior treatments
	- Surgery for selected cases, not responding to medical treatment or ophthalmologic complications	- Allergen-specific immunotherapy for clearly defined systemic hypersensitivity to an identified allergen
Severe	- Oral corticosteroids (short pulses) or corticosteroid lid injection for recalcitrant cases	- Advanced systemic treatments (such as immunomodulators) prescribed appropriately
		- Surgery for patients who may benefit from surgical intervention

## Hymenoptera Venom Allergy: An Overview

**Dr. Gilbert T. CHUA**

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### Introduction

Hymenopter venom allergy (HVA) is a significant public health concern that can lead to severe allergic reactions. In 2023 and 2024, two field workers of the Agriculture, Fisheries, and Conservation Department who worked in the country park passed away, suspected to be attributed to anaphylaxis following insect stings.(1, 2) This review discusses the types of insects associated with venom allergies, diagnostic approaches, emergency treatment, and an overview of venom immunotherapy.

### Common Insects Causing HVA

HVA primarily arises from the stings of certain insects, taxonomically divided into ants, bees, and wasps. In brief, common examples of bees include honey bees (*Apis mellifera*) and bumble bees (*Bombus sp.*); and wasps include Yellowjackets and hornets which are under the subfamily Vespidae, and paper wasps under the subfamily Polistinae.

### Diagnosis of Venom Allergy

Diagnosis of venom allergy typically involves a combination of clinical history, skin tests, and/or serum-specific IgE tests.

#### 1. Clinical History

A detailed clinical history is crucial for identifying potential allergens. Patients are asked about previous reactions to insect stings, including the type of insect involved, the severity of the reaction, and any history of anaphylaxis.

There are two types of clinical reactions – local reactions and systemic reactions.

- Local reactions refer to any responses where the signs and symptoms are restricted to the tissues surrounding the sting site. Most individuals experience only minor local reactions to Hymenoptera stings, which are not classified as

allergic reactions. In rarer cases, patients may develop large local reactions (LLRs). An LLR is characterized by painful swelling and redness confined to the skin and subcutaneous tissues adjacent to the sting site. The affected area is usually larger than 10 cm and can be significantly bigger. These reactions typically peak within 24 to 48 hours and can persist for 3 to 10 days.(3, 4)

- Systemic reactions are defined as signs and symptoms that occur away from the sting site and can manifest in a range of severity, from mild to life-threatening. These reactions can be categorized into two types: those that affect multiple organ systems (i.e. anaphylaxis) and those that are confined to the skin (cutaneous systemic reaction).(3, 4)

#### 2. Skin Tests or Serum-Specific IgE Tests

Skin prick tests are commonly employed to assess sensitivity to specific insect venoms. A positive reaction indicates the presence of specific IgE antibodies to the venom. In cases where skin testing is contraindicated, serum-specific IgE testing can be performed. This method is particularly useful for patients with a history of severe reactions or those on medications that may interfere with skin testing. Testing for venom IgE is not recommended in individuals with no history of sting reactions, as venom IgE can be detected in more than 20% of adults who have no history of reaction to stings, and the tests have poor positive predictive value. (4)

### Management of HVA

#### Emergency Treatment

Epinephrine is the first-line treatment for anaphylaxis. It should be administered intramuscularly as soon as anaphylaxis is suspected. Patients should be positioned appropriately, typically lying down with their legs elevated, to promote blood flow to vital organs. After

administering epinephrine, it is essential to call for emergency medical services. Patients should be monitored for recurrence of symptoms, as biphasic anaphylaxis can occur. Additional medications, including antihistamines and corticosteroids, may be administered as adjuncts, but they should not replace epinephrine as the primary treatment.(5)

### Venom Immunotherapy

Venom immunotherapy (VIT) is a well-established approach for treating individuals with severe allergic reactions to insect stings. Venom immunotherapy involves the gradual administration of increasing doses of venom, to desensitize the immune system. Typical VIT protocol involves an induction phase, which is the administration of escalating doses of venom over a period of several weeks; followed by a maintenance phase, in which the patient will receive regular doses of venom, typically every 4 to 6 weeks, and last for 3 to 5 years.(4)

### Indications for Venom Immunotherapy

VIT is indicated when the patient has a reliable history of anaphylaxis following an insect sting, and a positive venom skin test or elevated serum levels of venom-specific IgE. A positive venom skin test or the presence of venom-specific IgE but without a history of sting-induced anaphylaxis is **not** an indication for therapy, since approximately one-quarter of the general population has demonstrable venom-specific IgE.(4)

### Efficacy of Venom Immunotherapy (VIT)

VIT for honeybees, yellow jackets, hornets, and wasps is highly effective for subjects at risk of insect sting anaphylaxis. VIT reduces the risk of a subsequent systemic sting reaction down to 5%, compared with up to 60% in patients not receiving VIT. Subjects receiving VIT who experience systemic reactions after an insect sting generally have milder reactions than the reaction before VIT.(4, 6, 7) A recent study also revealed that, after a median of 4 years of VIT discontinuation, only 3.4% of subjects (5/147) who sustained re-sting post-VIT developed system reactions, indicating the long-term efficacy of VIT.(8)

### Conclusion

Venom allergy poses significant risks for affected individuals, necessitating prompt diagnosis and management. Understanding the types of insects responsible for venom allergies, recognizing the

symptoms, and implementing emergency treatment protocols can save lives. Venom immunotherapy offers a preventive approach for those at high risk of severe allergic reactions.

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### Effects of Different Cooking Treatments on Allergenicity of Cashew Nut

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In Hong Kong, where Chinese cultural roots intertwine with an embrace of Western living, there exists a historical practice of enjoying nuts as both snacks and gifts among its people, particularly during Chinese New Year. Additionally, cashews are commonly used as an ingredient in Chinese dishes.

Tree nuts are one of the most common food allergens. Allergic reactions to them can result in severe and occasionally life-threatening reactions. Tree nut allergies are increasing epidemiologically over time, particularly in children under the age of 18 years with self-reported prevalence 0.2% in 1997, 0.5% in 2002 and 1.1% in 2008. (1) In a recent systemic review of prevalence tree nut allergy in Europe, the lifetime self-reported prevalence was 0.9% and the point prevalence was 2.4%. (2) In Hong Kong, Leung et al reported (3) that tree nuts ranked the 6th most common food allergen with a prevalence of 0.41% in the total population and contributed to 5% of adverse food allergic reactions. There were increased hospitalisations for food-induced anaphylaxis including tree nuts, which attributed 3% hospitalisations. (4)

Numerous studies provide prevalence data on tree nut allergies, only a limited number of them specify information on individual nuts, such as cashew nuts. Like other tree nuts, the prevalence of allergies to cashew varies from region to region. In recent years, there appears to be an epidemiological rise in cashew nut allergies. Two studies from USA reported cashew as one of the most common tree nut allergies with a prevalence of 15% in 1999 and 30% in 2010. (5, 6) In a study conducted in Sweden, Johnson et al reported an estimated prevalence of cashew nut allergy at 6% among food allergies over a 10-year period (2001-2010). (7) The study further noted an increasing frequency and severity of allergic reactions to cashew nuts. In addition, Moneret-Vautrin et al showed an increase in the number of anaphylaxis cases caused by cashew nut allergy from 3% in 2003 to 9% in 2007 in France. (8)

We hypothesise that cooking treatments may enhance the tolerance of cashew nuts in allergic individuals. To date, three distinct groups of allergenic proteins in cashew nuts have been identified: Ana o 1, Ana o 2 and Ana o 3, which are all categorized as major allergens. Studies have shown that different types of processing can alter the allergenicity of food proteins. The objective of our study is to examine the impact of different cooking methods on the allergenic characteristics of cashew nuts. Cashews were subjected to five different cooking methods, which included boiling (100°C for 60-120mins), simmering (85-95°C for 60-120mins), baking (120°C for 90mins, 180°C for 20mins, 240°C for 11mins), stir-frying (low heat for 60mins, medium heat for 1.5mins, high heat for 0.5min) and air-frying (120°C for 90mins, 180°C for 8mins, 200°C for 5.5mins). To compare the electrophoretic profile of soluble protein extracts from the treated versus untreated cashews, we utilized SDS-PAGE (sodium dodecyl sulphate-polyacrylamide gel electrophoresis) for characterization.

Our findings revealed significant effects of specific cooking treatments on cashew nuts. Boiling for 120minutes, baking at 180°C for 20minutes and air-frying at 180 °C for 10minutes exhibited pronounced impacts by displaying less distinctive strained bands in the SDS-PAGE profile (Figure 1). Cashews exposed to specific temperatures for certain durations showed increased protein fragmentation, which does not necessarily correlate with higher temperatures or longer durations.

There have been a few studies describing the effect of different food processing treatments on the immunoreactivity of cashews in the literature. De Leon et al investigated the effect of roasting using patient sera and showed that there was no significant effect on IgE binding after roasting cashews at 180°C for 15minutes. (9) Su et al assessed the effect of gamma irradiation (1-25kGy) followed by thermal processing including autoclaving (121°C for 15-30mins), dry

roasting (160°C for 30mins, 177°C for 12mins), blanching (100°C for 5-10mins) oil roasting (191°C for 1min) and microwave heating (500W for 1-3mins). IgE binding with rabbit anti-cashew nut polyclonal antibodies was strongly reduced in cashew nut subjected to gamma irradiation at 25kGy followed by autoclaving at 121°C for 30minutes and roasting at 160°C for 30minutes. (10) Venkatachalam et al evaluated the effect of different processing including autoclaving (121°C for 5-30mins), blanching (100°C for 1-10mins), microwave heating (500 and 1000W for 1-2mins), dry roasting (140°C for up to 30mins, 170°C for up to 20mins, 200°C for up to 15mins), gamma-irradiation (1-25kGy) and pH(1-13). (11) Results illustrated that Ana o 1, Ana o 2 and Ana o 3 were stable regardless of the processing method to which the nut seeds were subjected. Autoclaving seems to have contradictory results and roasting shows limited effects on the allergenicity of cashew nut depending on the temperature and duration.

Interestingly, Venkatachalam et al (11) showed an overall increase in the intensity of the bands, indicating heightened immunoreactivity, in samples exposed to roasting at a temperature of 170°C for 20mins. Additionally, our study found that stir-frying at high heat and simmering increased the intensity of the bands in the SDS-PAGE profile. These results suggest that specific processing conditions such as high temperature may enhance, rather than diminish, the immunoreactivity of allergens present in cashew nuts.

Oral immunotherapy is now a treatment option for patients with cashew nut allergy. The NUT CRACKER study demonstrated that cashew oral immunotherapy desensitizes most cashew-allergic patients, with 88% of patients tolerating the target dose at the end of the study. However, 6% of patients required treatment with injectable epinephrine for home reactions. (12) Nonetheless, safety concerns, such as adverse reactions including anaphylaxis, make paediatric oral immunotherapy a controversial therapy. Cooking treatments may offer a safer approach for introducing cashew nuts with reduced allergenicity to patients with allergies. Further research is required to explore the complex relationships between the effects of different cooking treatments on the allergenicity of food proteins and the establishment of a "safe" level of allergenicity necessary for successful oral immunotherapy.

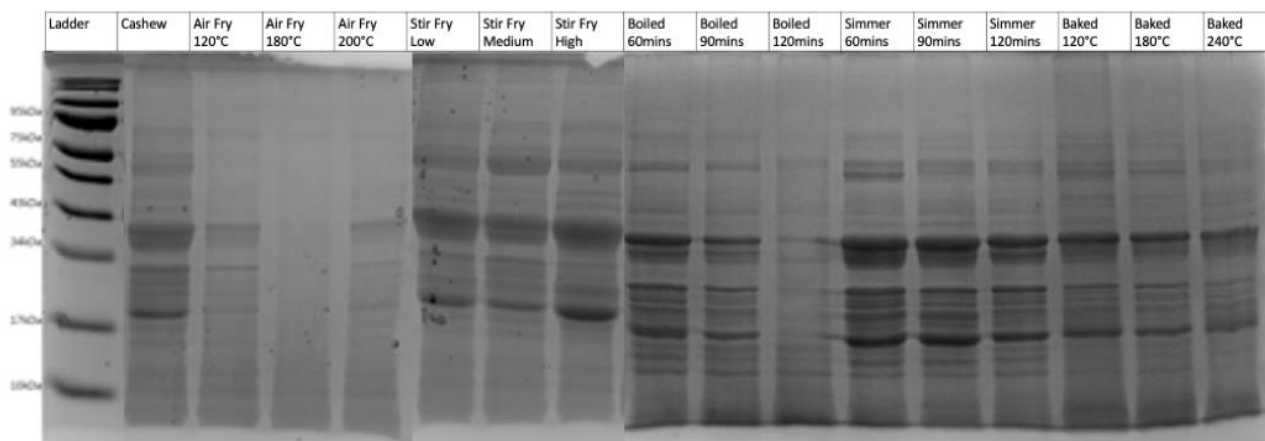
Acknowledgment: We thank the support of the Hong Kong Institute of Allergy for our research.

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Figure 1. The SDS-PAGE analysis of the raw and treated cashew nuts.



## ADHD and Atopic Diseases: The Inflammatory Correlation

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Recent Studies in Neuroscience and Psychology suggests a pathophysiological relationship between inflammation and Attention-deficit/hyperactivity disorder (ADHD) including peripheral inflammatory diseases such as Atopic dermatitis.<sup>1</sup> Studies suggest the relationship between cytokine levels, neurophysiological function and behavioral manifestation in Atopic Diseases and ADHD.<sup>9</sup>

In studies comparing adults and children, presence of Atopic dermatitis related to a significant association in symptom severity of ADHD including hyperactivity/impulsivity and inattention. A causal association was suggested.<sup>5</sup>

Recent studies have documented inflammatory cytokines linked to Atopic diseases to also be significantly elevated in ADHD Table 1.

### The Inflammatory Cytokine Scenario

While raised IL-1Beta level was linked to poor motor skills, Children with higher IL-6 showed frequent inattention, aggression. IL-6 serum levels were significantly raised in ADHD vs Controls 22.35 [95%CI (17.68-26.99)] vs. 5.44 [95%CI (4.81-6.06)].<sup>11,7</sup>

Anatomical and physiological evidence shows evidence of intense communication between neuroendocrine mediators, nerve fibers and immune cells in Atopic Dermatitis.<sup>9</sup>

### Inflammatory Cytokines in Pruritus, Sleep Deprivation and Attention Issues

Sleep disturbances from intense pruritus in Atopic Dermatitis is known to amplify stress and related inflammatory biomarkers. Higher levels on inflammatory cytokines mediate peripheral pruritus and communication to the CNS, induces cytokine activity in the brain. This is known to cause reduced REM sleep which is linked to reduction in cognitive skills such as working memory, sustained attention, executive function and processing speed.<sup>2</sup>

A large cross-sectional study of 354,416 children age 2-17 yrs. found Atopic Dermatitis increased odds of ADHD

including loss of sleep being an aggravating factor. Further studies found insomnia, asthma and headaches increased the odds of an ADD diagnosis in adults.<sup>10</sup>

The higher inflammatory molecules in eczema may increase action potential frequency in the peripheral nerves causing increased amounts of neurotransmitter release at the spinal level further causing abnormal neuropathy and sensory functions leading to hyperkinesia. Neuropeptides may regulate functions of mast cells, dendritic cells, eosinophils and T cells contributing to the cycle.<sup>2</sup>

Homeostasis in the CNS is dependent on equilibrium of the innate, adaptive immune system, neurons and glial cells. Inflammation anywhere in the body impacts cognitive function and behavior as seen in 'sickness behavior' during acute illness thought to be evolutionary protective. Chronic inflammation and infection can cause neurodegeneration and neurotoxicity.<sup>2</sup>

In conclusion the evidence of similar pathophysiology and association between inflammatory biomarkers in Atopic diseases and ADHD is mounting.

Clinicians especially family physicians, specialists in mental health, paediatrics, allergists and dermatologists should consider the possibility of co-morbidity of Atopic disease and ADHD while also paying attention to pruritus and sleep. A multispecialty approach may support early identification and monitoring of vulnerable groups. Early diagnosis and intervention would support improved QoL and long-term outcomes.

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**Table 1. Bio-Markers of Inflammation commonly raised in Atopic Diseases Documented as raised in Attention Disorders**

<b>Inflammatory markers documented to be raised in Atopic diseases, Allergies and ADHD</b>
CRP-hs <sup>3</sup>
Eosinophils <sup>8</sup>
IgE, TNF-alpha <sup>6</sup>
IL-6 <sup>1</sup>
IL-1Beta <sup>11</sup>
IL17 <sup>9</sup>
IL-4, IL-13, IL-31 <sup>2</sup>

## Annual General Meeting 2024 26 November 2024

The Annual General Meeting for this year took place on 26 November 2024 at The Hong Kong Country Club. Council members and a number of members enjoyed the evening. Congratulations to the following doctors who were elected to significant roles for the upcoming year:

- Professor Philip Li: President
- Dr. Agnes Leung: Vice President
- Dr. Marco Ho: Honorary Treasurer
- Dr. Jane Chan: Council member

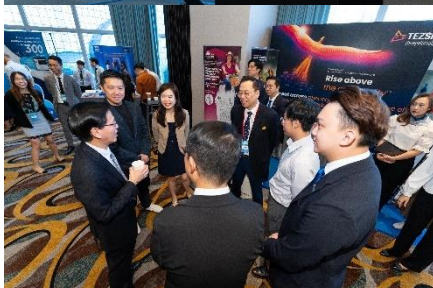
We would like to take this opportunity to express our sincere gratitude to our Immediate Past President, Professor Gary Wong for his contributions and leadership during his four-year tenure. We are confident that our Council and Committee members will continue to guide our institution towards further milestones.



## Hong Kong Institute of Allergy Annual Scientific Meeting (HKIA ASM 2024) 6 October 2024

The Hong Kong Institute of Allergy Annual Scientific Meeting was successfully held on 6 October 2024 at the Hong Kong Convention and Exhibition Centre with over 150 healthcare professionals participating in this event. The Theme for this year's ASM was "A New Era of Allergies Prevention", focused on the latest discoveries in the mechanisms, cutting-edge treatments, and preventive strategies for allergic diseases. The program encompassed discussions on Anaphylaxis, Asthma, Eczema, Food Allergy, Immunology and Allergy, Wheezing Disorders, and Practical Sessions on Aeroallergen Tests.

The Organizing Committee would also like to extend their heartfelt gratitude to all the speakers, supporting organizations, and sponsors for their unwavering support.



## Overseas Meetings

### AAAAI / WAO Joint Congress 2025

(The American Academy of Allergy, Asthma & Immunology and World Allergy Organization Joint Congress 2025)  
28 Feb – 3 Mar 2025 / San Diego, USA (<https://annualmeeting.aaaai.org/>)

### EAACI Congress 2025 (European Academy of Allergy and Clinical Immunology 2025)

13 – 16 June 2025 / Glasgow, Scotland ([https://eaaci.org/events\\_congress/eaaci-congress-2025/](https://eaaci.org/events_congress/eaaci-congress-2025/))

## Local Meeting

### HKTS / CHEST Annual Scientific Meeting 2024 (ASM 2025)

23 March 2025 / Hong Kong