THE HONG KONG 香 港 醫 訊
MEDICAL DIARY
www.fmshk.org
VOL.20 NO.5 May 2015

Allergy in Hong Kong

OFFICIAL PUBLICATION FOR THE FEDERATION OF MEDICAL SOCIETIES OF HONG KONG ISSN 1812 - 1691

YOU ARE INVITED

The All - New Maserati Quattroporte Elite is now available. You are invited to get behind the wheel to experience the Italian touch of luxury and aesthetics.

Be the first to enjoy an exclusive test drive day in our brand new Maserati Flagship Showroom with superb purchase privileges*. Light refreshment and children's delights will be served. Come join us along with your family and friends!

Event details:

Date: 17th May, 2015 (Sunday)

Time: 11am to 5pm

Venue: Maserati Flagship Showroom
First Group Centre, No.14 Wang Tai Road, Kowloon Bay

For reservation, please contact 2527 8898 or email to info@fmshk.org

AUTO ITALIA LTD.

UNITS A-C, G/F, NEICH TOWER, 128 GLOUCESTER ROAD, WAN CHAI, HONG KONG

60 REPULSE BAY ROAD, REPULSE BAY, HONG KONG

Tel: 2627 8900

E-mail: sales@maserati.com.hk

Quattroporte Elite from $1,388,000

* Purchase privileges for selected stock only.

www.maserati.com.hk

Join us on Facebook and WeChat

Maserati Hong Kong

Contents

Scan the QR-code

To read more about The Federation of Medical Societies of Hong Kong

Disclaimer

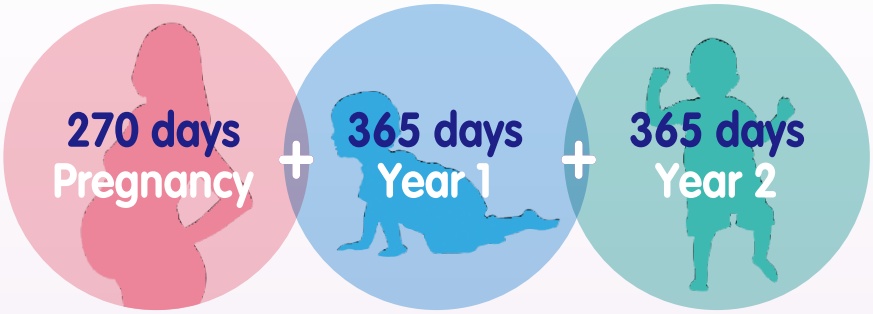
The Cover Shot

An allergy collage of some examples of common allergic conditions, allergens and diagnostic tests.

Mr Johnny KC WONG

Nestlé
Start Healthy
Stay Healthy

First 1,000 days Nutrition for a better life



- ✓ 100% whey partially hydrolyzed formula (PHF-W) is clinically proven [1-3]
- ✓ PHF-W reduces the risk of atopic dermatitis in infants with family history of allergy in the first year of life by up to 50% as proven by two recent meta-analyses [1,3]
- GINI
- ✓ Protective effect of PHF-W confirmed until the age of 10 years up to 33% in the German Infant Nutritional Intervention Study [2]
- ✓ 100% whey partially hydrolyzed formula recommended by international pediatric associations when exclusive breastfeeding is not possible [4-6]
- ✓ With unique Nestlé OPTIPRO® technology - provide optimal protein quality & quantity
- ✓ Helps in reducing allergenicity of cow's milk protein [7]

IMPORTANT NOTICE: The World Health Organization recommends exclusive breastfeeding for 6 months. Nestlé fully supports this and continued breastfeeding, along with the introduction of complementary foods as advised by your doctor or health authority.

NESTLÉ® NAN® PRO 2 is a follow-up formula for babies from 6-12 months old. It is not a breast milk substitute. NESTLÉ® NAN® PRO 2 has been formulated for use as a nutritional supplement for the transition to the semi-solid and solid food portion of the older infant's diet.
NESTLÉ® NAN® PRO 3 and NESTLÉ® NAN® PRO KID 4 are not breast milk substitutes but a growing-up milk specially suited to healthy young children aged from 1-3 years old and from 3 years old respectively.

REFERENCE:
1. Szajewska H, Horvath A. Curr Med Res Opin. 2010;26(2):423-37.
2. Von Berg A. et al. J. Allergy Clin Immunol 2013.
3. Alexander D, Cabana M. JPGN 2010;50(4):422-30.
4. Høst A, Koletzko B, Dreborg S et al. Arch Dis Child. 1999;81(1):80-4.
5. Høst A, Halken S, Muraro A et al. Pediatr Allergy Immunol 2008:19(1):1-4.
6. Chouraqui JP, Dupont C, Bocquet A et al. Arch Pediatr 2008;15(4):431-42.
7. Muraro A et al. Pediatric Allergy and Immunology 2004; 15(3) : 196-205.

www.nestle.com.hk

Why Are Allergists Needed in Hong Kong?

Dr Tak-hong LEE

Dr Tak-hong LEE

MBBChir, MD, ScD, FRCP, FRCPath, FHKCP
Director, Allergy Centre, HK Sanatorium and Hospital

Editor

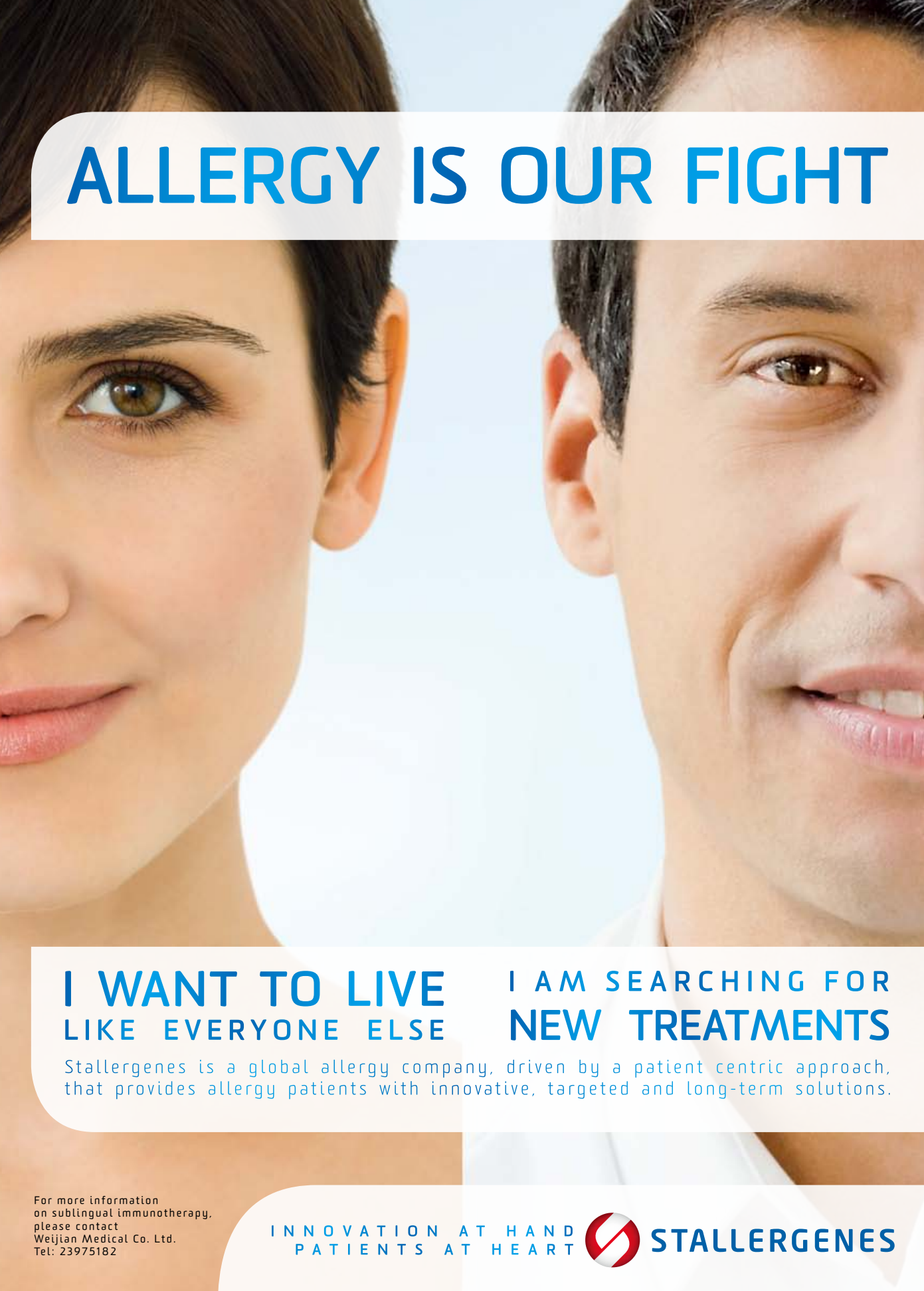
Allergic diseases are amongst the commonest chronic non-communicable diseases in the world. Many children in Hong Kong have allergies and the rate of the potentially fatal anaphylaxis is high. There is a rising trend for many allergic disorders and only a minority of children will grow out of their allergies so the problem could last a life time. It is therefore of grave concern that there are so few allergy specialists in HK, which boasts an otherwise mostly excellent health care environment.

This issue of the Medical Diary summarises the epidemiology of allergic diseases in HK. It highlights the severe deficiencies in service provision and training as already described in a recent authoritative review written on behalf of the Hong Kong Allergy Alliance[1]. It explains why more Allergists are required and suggests ways to remedy the situation. This issue then describes several unique areas where an Allergist can make a significant contribution to HK's health care with an update of a new tool in molecular allergology for allergy diagnosis.

We hope readers will find the articles informative and interesting. An explosion of new knowledge on the mechanisms of immunological tolerance; introduction of novel biologics for allergic diseases; the development of safer allergen-specific vaccines; and the inevitable advent of stratified medicine demand the need for more specialists trained to manage and prevent allergic diseases.

References

1. Chan YT, Ho HK, Lai CKW, Lau CS, Lau YL, Lee TH, Leung TF, Wong GWK, Wu YY. Allergy in Hong Kong – an unmet need in service provision and training. The Hong Kong Medical Journal 2015;21:52–60


ALLERGY IS OUR FIGHT
I WANT TO LIVE
LIKE EVERYONE ELSE
I AM SEARCHING FOR
NEW TREATMENTS
Stallergenes is a global allergy company, driven by a patient centric approach, that provides allergy patients with innovative, targeted and long-term solutions.
For more information
on sublingual immunotherapy,
please contact
Weijian Medical Co. Ltd.
Tel: 23975182
INNOVATION AT HAND
PATIENTS AT HEART
STALLERGENES

How common are allergies in Hong Kong ?

Prof Gary WK WONG
MD, FRCPC
Department of Paediatrics, Prince of Wales Hospital, Chinese University of Hong Kong

Prof Ting Fan LEUNG
MBChB, MD, FRCPCH
Department of Paediatrics, Prince of Wales Hospital, Chinese University of Hong Kong


Prof Gary WK WONG Prof Ting Fan LEUNG

Introduction

Allergies are among the most common chronic conditions affecting adults and children. The correct determination of the prevalence of allergic conditions is complicated. Many studies from around the world have been conducted over the past few decades. The majority of them used simple questionnaires without proper validation making it difficult to estimate the true prevalence of various allergic conditions. There have been many epidemiology studies conducted in Hong Kong over the past twenty years. Most of the studies were conducted on children because it is relatively easy to obtain a random sample of children for estimation of various allergic conditions. Among the different epidemiology studies of allergic disorders, many were aiming at determining the prevalence and risk factors of asthma. There have also been studies evaluating the prevalence of allergic rhinitis and food allergies conducted in Hong Kong.

Prevalences

The International Study of Asthma and Allergies (ISAAC) was the largest epidemiology study of childhood asthma and allergies. Phase I of ISAAC used standardised and validated questionnaires to measure the prevalence of childhood asthma, allergic rhinitis and atopic eczema for international comparison. The ISAAC studies were conducted in three phases. Phase I obtained baseline prevalence data for subsequent comparison. Phase II was an in-depth study of the important risk factors for asthma. Phase III was a repetition of Phase I to assess the possible changing trend of asthma and related allergic conditions. Random samples of school children aged 6-7 years and 13-14 years were recruited for Phase I and III studies.

Phase I was conducted in Hong Kong in 1995[1]. Among children aged 13-14 years, the prevalence of physician diagnosis of asthma ever was 11%, symptoms of rhinoconjunctivitis in the preceding 12 months was 26%, and symptoms of flexural eczema in the preceding 12 months was 3.1%. Phase III was conducted in 2002, the results revealed that the prevalence of asthma was 10.2% and the difference between Phase I and Phase III was not statistically significant[2]. It was reassuring that the severity of asthma symptoms has reduced among those with a physician diagnosis of asthma in 2002 when compared with those in 1995.

Phase II study was conducted in children aged 9-11 years[3]. The prevalence of physician diagnosis of asthma ever was 9.6%, symptoms of rhinoconjunctivitis in the preceding 12 months was 16.8%, and symptoms of flexural eczema in the preceding 12 months was 5.3%. Another study of asthma and allergies in preschool children aged 2-6 years was conducted in 2006. The prevalence rates of physician diagnosis of asthma, symptoms of rhinoconjunctivits and symptoms of flexural eczema were 4.9%, 11.8%, and 5.6% respectively. The results of these studies suggested that asthma, allergic rhinitis and eczema are common. One in three children is suffering from at least one of these allergic conditions. However, the prevalence of these conditions appears to have stabilised over the past 10 years.

In order to assess the level of control among asthmatics in Asia-Pacific, the Asthma in Reality in Asia-Pacific (AIRIAP) study was performed twice in Asian countries. Both studies revealed that a very small proportion of asthmatics achieved control of their asthma as defined by GINA[4]. The results from AIRIAP II conducted in 1996 showed that only 2.9% had 'controlled' asthma while 34.7% had 'uncontrolled asthma'. Among children younger than 16 years old, only 2.5% had 'controlled asthma' while 53.4% had 'uncontrolled asthma'[5]. The over reliance on short-acting bronchodilators and underuse of inhaled corticosteroids were found to be major factors associated with poor control of asthma.

There have also been a few studies examining the prevalence of food allergies in Hong Kong. Compared to asthma, an accurate determination of the prevalence of food allergies is much more difficult. Many people may report symptoms suggestive of food allergies but a large proportion of them would be found not to have food allergies by objective testing such as food challenge tests. In 2009, a questionnaire-based study among preschool children aged 2-7 years old showed that 8.1% were reported to have adverse food reactions by their parents[6]. The most commonly reported allergens were shellfish, milk and egg. Another questionnaire-based study of children from birth to 14 years showed a prevalence of food allergy of 4.8%[7]. The Europrevall survey used standardised methodology along with the use of objective testing such as a skin-prick test and measurement of serum specific IgE and detailed assessment of the food reactions to study children from many countries in Europe, China, India, and Russia[8]. Children aged 7-10 years were studied. Among children who were recruited from Hong Kong, 2.8% were found to have 'probable' food allergy defined by having symptoms compatible with food allergies occurring within 2 hours of ingestion along with positive

sensitisation to the specific food. A study of adults and children presented to emergency with anaphylaxis showed that 49.6% were due to food allergy among those with an obvious precipitant. These data suggested that food allergy and food induced anaphylaxis are significant problems. Given the experience of an increase in the prevalence of food allergies as the 'second wave' of the allergic epidemic, it is likely that the prevalence of food allergy will increase in Hong Kong over the next 10 to 20 years[9].

Risk Factors

In order to determine the possible risk factors associated with the development of asthma and related allergies in the Chinese population, there have been many collaborative studies using the same methodologies evaluating subjects recruited from Hong Kong and different parts of the China Mainland. Children who were born in the Mainland and migrated to Hong Kong were found to have much lower prevalences of asthma and allergies. ISAAC Phase II showed that those children born and raised in Hong Kong had a prevalence of physician diagnosis of asthma of 8.6% whole those born in the Mainland and migrated to Hong Kong subsequently only had a prevalence of 2.1%. Furthermore, the prevalence of allergic sensitisation to common aeroallergens was 42.9% among children born and raised in Hong Kong compared with only 22% in children born in the Mainland[3]. Several environmental factors and dietary factors were associated with the protection against the development of asthma and allergies[10]. Mechanistic studies are needed to evaluate if these factors are causal in their relationship with asthma.

Conclusion

One in three children in Hong Kong suffered from at least one allergic condition with asthma and allergic rhinitis being the most common conditions. The prevalence of asthma in children seems to have stabilised while that of food allergies may be increasing. More studies are needed to determine the prevalence of allergic conditions in adults. Given such a large burden of allergic diseases in children and adults, adequate allocation of resources and training of specialists in the field are necessary to manage these potentially fatal conditions.

References

1. Leung R, Wong GW, Lau J, Ho A, Chan JK, Choy D, Douglass C, Lai CK. Prevalence of asthma and allergy in Hong Kong schoolchildren: an ISAAC study. Eur Respir J 1997;10:354-60.
2. Wong GW, Leung TF, Ko FW, Lee KK, Lam P, Hui DS, Fok TF, Lai CK. Declining asthma prevalence in Hong Kong Chinese schoolchildren. Clin Exp Allergy 2004;34:1550-5.
3. Wong GW, Hui DS, Chan HH, Fok TF, Leung R, Zhong NS, Chen YZ, Lai CK. Prevalence of respiratory and atopic disorders in Chinese schoolchildren. Clin Exp Allergy 2001;31:1225-31.
4. Ko FW, Leung TF, Hui DS, Chu HY, Wong GW, Wong E, Tung AH, Lai CK. Asthma Control Test correlates well with the treatment decisions made by asthma specialists. Respirology 2009;14:559-66.
5. Wong GW, Kwon N, Hong JG, Hsu JY, Gunasekera KD. Pediatric asthma control in Asia: phase 2 of the Asthma Insights and Reality in Asia-Pacific (AIRIAP 2) survey. Allergy 2013;68:524-30.
6. Leung TF, Yung E, Wong YS, Lam CW, Wong GW. Parent-reported adverse food reactions in Hong Kong Chinese preschoolers: epidemiology, clinical spectrum and risk factors. Pediatr Allergy Immunol 2009;20:339-46.
7. Ho MH, Lee SL, Wong WH, Ip P, Lau YL. Prevalence of self reported food allergy in Hong Kong children and teens—a population survey. Asian Pac J Allergy Immunol 2012;30:275-84.
8. Wong GW, Mahesh PA, Ogorodova L, Leung TF, Fedorova O, Holla AD, Fernandez-Rivas M, Clare Mills EN, Kummeling I, van Ree R, Yazdanbakhsh M and Burney P. The EuroPrevall-INCO surveys on the prevalence of food allergies in children from China, India and Russia: the study methodology. Allergy 2010;65:385-90.
9. Prescott S, Allen KJ. Food allergy: riding the second wave of the allergy epidemic. Pediatr Allergy Immunol 2011;22:155-60.
10. Wong GW, Ko FW, Hui DS, Fok TF, Carr D, von Mutius E, Zhong NS, Chen YZ, Lai CK. Factors associated with difference in prevalence of asthma in children from three cities in China: multicentre epidemiological survey. BMJ 2004;329:486-9.

Under Provision of Allergy Services and Training in Hong Kong

Dr YT CHAN[1], Dr HK HO[2], Dr CKW LAI[3], Prof CS LAU[4], Prof YL LAU[2], Dr TH LEE[5], Prof TF LEUNG[6], Prof GWK WONG[6], Dr YY WU[7]

(Authors listed alphabetically)

On behalf of the Hong Kong Allergy Alliance and the Hong Kong Institute of Allergy

[1] *Specialist in Immunology; Division of Clinical Immunology, Department of Pathology and Clinical Biochemistry, Queen Mary Hospital.*
[2] *Specialist in Paediatric Immunology and Infectious Diseases; Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, the University of Hong Kong*
[3] *Specialist in Respiratory Medicine; private practice*
[4] *Specialist in Rheumatology; Division of Rheumatology and Clinical Immunology, Department of Medicine, the University of Hong Kong*
[5] *Specialist in Immunology and Allergy; HK Sanatorium and Hospital*
[6] *Specialist in Paediatrics; Department of Paediatrics, The Chinese University of Hong Kong, Prince of Wales Hospital*
[7] *Specialist in Immunology and Allergy; private practice*

DECLARATIONS OF INTEREST

CKW Lai, CS Lau, TF Leung, YY Wu are consultants or serving on advisory boards and/or receiving travel expenses and lecture fees to attend international meetings from various pharmaceutical companies including GlaxoSmithKline, AstraZeneca, Takeda, Mundipharma, Boehringer, ALK-Abello, AbbVie, Bristol-Myers Squibb, Celltrion, Janssen, Novartis, Pfizer, Roche, Sanofi, and Union Chimique Belge. TH Lee is President of the Hong Kong Institute of Allergy and Honorary Clinical Professor, the University of Hong Kong. Dr Marco Ho is Chairman of Allergy HK.

The Allergy Alliance is a group of individuals with an interest in allergy drawn from the academia; HA hospitals; private practitioners; representative from HA; Hong Kong Institute of Allergy; HK Thoracic Society; Allergy HK; patients and drug company representatives from ALK.

Introduction

Allergic diseases are amongst the commonest chronic non-communicable diseases in the world. Many children in HK have allergies and the rate of potentially fatal anaphylaxis is high (700/100,000 of the population aged 14 years or less)[1]. There is a rising trend for many allergic disorders and only a minority of children will grow out of their allergies so the problem could last a life time. Unfortunately Hong Kong's health care does not match the disease burden and there is a major service gap.

A group of clinicians, allied health professionals and others with an interest in Allergy met in March 2014 (now named "The Hong Kong Allergy Alliance") and agreed that an authoritative review about allergy in HK should be written so that informed discussions could be undertaken with major stakeholders to try and remedy the deficiency.

This brief review summarises the key findings of the report which can be found on http://www.allergy.org.hk/new/subcommittee.html and is published in the HK Medical Journal1.

The evidence for unmet needs

It is estimated that in HK there is about [1] Allergist : 1.46 million head of population, which is low compared to international figures. The ratio of paediatric Allergists per head of population is around 1:460,000 and that for adult patients is 1: 2.8 million, so there is a severe lack of adult Allergists. Paediatric Allergists only spend a fraction of their time on allergy.

There are no Allergists in adult medicine in public hospitals and many allergic patients are seen by General Practitioners and non-specialists in Allergy. Waiting times for even the simplest of all allergy testing such as skin prick testing can be 6 months so the demand for Allergists and Allergy services are unmet. The Paediatric Immunology and Infectious Disease (PIID) specialty that includes Allergy has made progress and developed a network of four contributing Centres but the service is still limited by insufficient manpower. Finally a vibrant allergy service must be supported by a robust immunological laboratory, but the laboratory support for Allergy/ Immunology in the public sector cannot offer a complete portfolio of allergy tests because of insufficient resources.

Drug allergies can impact on the practice of medicine by many specialties but there are very few drug allergy clinics in HK. There are also very few local guidelines for managing allergic diseases. The use of allergen immunotherapy which is an essential tool in allergy treatment is very limited in HK.

If the current situation in HK is bad enough, the future is even bleaker. There have been no trainees in Allergy and Immunology in adult medicine since 1998. Training in adult Allergy is hampered by the lack of trainers and the virtually non-existence of an Allergy clinical service in the public sector.

Why are Allergists needed?

First, most patients with allergies have multi-system involvement, for example a child with food allergies could present with asthma, rhinitis, eczema, abdominal pain and anaphylaxis at the same time. This could involve the patient consulting multiple specialists at great inconvenience and expense. This could be avoided by streamlining care under one Allergy-trained specialist ("one-stop-shop") making it easier for patients and often saving on resources. The Allergist's approach aims to correct the underlying cause and they can help patients understand how to prevent allergic diseases from developing.

Second, in the absence of Allergists patients may suffer because they may find it hard to get state-of-the-art medicine and diagnostics.

Third, unproven diagnostic procedures and therapies could be introduced if mainstream medicine is unavailable, or conventional tests could be used / interpreted inappropriately. For instance it is often

erroneously believed that a positive skin prick test to an antigen equates to allergy, when it actually signifies sensitisation to that allergen and not necessarily allergy.

Fourth, if there is a lack of Allergy specialists, it becomes difficult to train future generation of clinicians, researchers and teachers in allergy.

Fifth, there is little time or capacity to generate new knowledge to advance the understanding of allergic diseases and develop novel approaches to therapy, because the clinical burden is so heavy for the few Allergists that exist.

Suggestions for the way forward

We recommend that the deficiencies in Allergy service provision and training should be remedied as soon as possible. We suggest that the best model for Allergy service delivery is a "hub and spokes" model[1]. The "hub" would act as a central point of expertise with outreach clinical services, education and training provided to doctors, nurses and allied health professionals in primary and secondary care (the "spokes"). In this way, knowledge regarding the diagnosis and management of allergic conditions could be disseminated throughout the region. The hub and spokes in its entirety form the "Allergy Centre". The hub should lead and coordinate the activities of the entire Centre.

Each hub should be led by an Allergy specialist supported by another Allergy specialist or an organ specialist with a special interest in Allergy, at least one trainee, a specialist dietitian, a specialist nurse and a technician for routine allergy testing, counselling and education.

In addition a network of satellite allergy services (spokes) could be established at other hospitals (for instance by allocating new resources, or more likely by changing the emphasis of one or two existing clinic settings a week in related disciplines to become Allergy clinics). These Allergy clinics can then link to one of the Allergy hubs for academic, clinical and educational support. This solution might not require many more resources as the complex multi-system allergy cases from the other clinics can be collected up for management in a new dedicated Allergy service.

It is important to emphasise that Allergy Centres will be collaborating and not competing with single organ specialists or with general paediatricians, internists and general practitioners. The Centres would work together with other colleagues to provide a joint, integrated and holistic care for the more complex allergy cases. To facilitate this interaction, the criteria for referrals to specialised Allergy Centres should be clearly defined as have been done in other countries[2].

Adult allergy requires urgent resuscitation. We recommend that two pilot Allergy Centres are created and an Allergy specialist is recruited (from overseas if necessary) to each Centre to kick start the adult service and to oversee a training and research programme. The two pilot Allergy Centres could be located at the Queen Mary Hospital/HKU and the Prince of Wales Hospital/CUHK (hubs), so that Hong Kong, Kowloon and the New Territories are covered. Creation of an Allergy Centre that integrates existing strengths in paediatric clinical/academic/education in allergy with a new adult clinical/academic/education allergy service would help to fill the obvious gaps in service and academic provision.

We recommend that intercollegiate training programmes in Immunology and Allergy combined with a College specific programme could be considered, for example between the HK College of Pathologists and HK College of Physicians to produce Clinical Immunologists who will direct Allergy/Immunology laboratories and consult for allergic patients.

When the HK Children Hospital (HKCH) is operational it could contain a "hub" Paediatric Allergy Centre. In the meantime it will be essential to put in place the necessary numbers of trainees and specialists in readiness to staff the top tier service and to provide secondary services as described previously[1].

Drug Allergy is common and constitutes a major clinical problem, which is best managed by Allergy specialists. We recommend resources to be made available to establish two separate supra-regional Drug Allergy Services at QMH and PWH (as they already have a limited service) to cover Hong Kong Island and Kowloon/New Territories. This could be part of the new pilot Centres.

We recommend that two supra-regional labs for HK should be created with a focus on drug and food allergies that are directed by accredited Immunologists. These can be incorporated into existing laboratory support at QMH and PWH with only a relatively modest increase in resources. They could then support the new pilot Centres.

While the report concentrates on allergy services because of the large volume of patients, it should be noted that the discipline is Immunology and Allergy. The volume of immunological work, e.g. in primary immunodeficiencies is lower volume than for allergy but it is much more labour intensive. Unfortunately the provision of immunological services in HK is also lagging behind international standards. Currently there is no continuum of care; for instance there is no seamless transfer of care from paediatricians to adult physicians in primary immunodeficiencies. HK also urgently needs a visionary strategy to remedy this situation.

Conclusion

The provision of services and training for Specialists in allergy in HK are mismatched with disease burden. There is a large unmet need which needs to be remedied proactively without delay before a series of clinical disasters strike and an urgent solution has to be found reactively. Key recommendations are proposed which could help bridge the gaps, including the creation of two pilot Allergy Centres in a hub and spoke model in the public sector.

References

1. Chan YT, Ho HK, Lai CKW, Lau CS, Lau YL, Lee TH, Leung TF, Wong GWK, Wu YY. Allergy in Hong Kong – an unmet need in service provision and training. The Hong Kong Medical Journal 2015;21:52–60
2. http://www.england.nhs.uk/wp-content/uploads/2013/06/b09-spec-allergy.pdf

Overview of allergy prevention strategies

Dr Alson WM CHAN

MBChB, DCH (Ireland), Dip Ger Med RCPS (Glasg), PdipCommunityGeriatrics, MRCPCH, FHKCPaed, FHKAM (Paed)

Specialist in Paediatrics

Dr Alson WM CHAN

Introduction

The increasing prevalence of allergic diseases has continued in the last 50 years, and children account for the main burden of the rise. The sensitisation rates to one or more common allergens among school age children are approaching 40-50%.[1] The growing burden of allergic diseases in many developed and developing countries has been recognised as a pandemic in the 21st century and there is a pressing need for effective allergy prevention strategies.[2]

Pregnancy and lactation period

Some studies suggested a critical time early in the foetal or infant period when there is a higher chance for developing sensitisation, so dietary interventions have been investigated.[3] But recent systematic reviews on randomised trials have found that there is still insufficient evidence to advise women for dietary modifications during pregnancy or lactation.[4] Moreover it may adversely affect maternal and infant nutrition.

Milk feeding

Breast milk is the best source of nutrition for newborns during the first six months of life, regardless of their atopic tendency.[5] Infants on breastfeeding have less frequent recurrent wheezing,[6] a lower incidence of eczema[7] and a decreased risk of cow's milk protein allergy.[8] It was also shown to reduce the risk of allergic rhinitis, although just statistically insignificant (odds ratio =0.74; 95% CI 0.54-1.01).[9]

For normal infants, there is no convincing evidence to suggest any one formula provides more advantages than the others. However, for high-risk infants if they could not be completely breastfed, those who received hydrolysed formulas had a lower risk of developing eczema, cow's milk protein allergy and other atopic diseases when compared with those on conventional cow's milk formulas.[10] Studies have shown a slight benefit of extensively hydrolysed formulas compared with partially hydrolysed formulas,[11] although the cost and palatability of the former are the main drawbacks. Soy formulas were not shown to have any role in allergy prevention and no major study has addressed the effect of amino acid based formulas.

Solid food introduction

Population-based prospective birth cohorts revealed that delaying the introduction of solid foods before four months or later than six months of age increased the risk of allergic diseases.[12] The European Food Safety Authority concluded that the safe period for the introduction of complementary foods is between four to six months in healthy full-term infants.[13] The American Academy of Pediatrics supports the introduction of complementary foods after at least four months of age.[14] Latest birth cohorts have shown that more diversity of food at one year of age has a protective effect from allergic diseases.[15]

Highly allergenic foods such as egg, peanut, tree nuts, dairy products (other than cow's milk), fish, and shellfish can be gradually introduced to infants who have tolerated a few less allergenic foods, but cow's milk should be avoided until one year for other reasons not related to allergy.[16] In the case of an infant who has developed any allergic reaction to a food, or already has moderate to severe atopic eczema, referral to a specialist for testing and monitoring is recommended for advice on the introduction of highly allergenic foods.

Prebiotics & probiotics

Prebiotics are nondigestible carbohydrates stimulating the growth of beneficial intestinal bacteria. Probiotics are live microorganisms promoting the health status of the host. Synbiotics are a combination of both.

Pre-clinical studies have revealed that the spectrum of the intestinal flora might modulate the immune status of the host and decrease allergic inflammation.[17] Several meta-analyses have shown a significant reduction in eczema when probiotics were prescribed pre- and postnatally.[18] Recently, the World Allergy Organization guideline panel suggests using probiotics in pregnant women at high risk for having an allergic child; in women who breastfeed infants who are at high risk of developing allergy; and in infants at high risk of developing allergy. [19]

Concerning prebiotics, meta-analyses have shown their safety profile.[20] But more studies are needed to investigate the efficacy of prebiotics and synbiotics in clinical settings.

Environment & lifestyle

Prevention from cigarette smoke exposure is an effective strategy in preventing allergic airway diseases. Passive exposures to cigarette smoke prenatally and in childhood led to a twenty percent increase in the incidence of allergic diseases. A dose-response relationship has been demonstrated.[21] Children with prenatal exposures only are already at higher risks.[22] Exposures in the first year of life have a stronger effect than subsequent exposures, suggesting that the infantile period is a particularly vulnerable time.[23]

Air pollutant exposures also increase the risk of asthma exacerbations and impair lung functions.[24] Exposure to antibiotics in early life is associated with an increased risk of asthma and allergic rhinitis.[25] Furthermore, obesity has been shown to be associated with asthma.[26] Cochrane meta-analysis suggested that multifaceted interventions including both environment and diet strategies decreased the risk of asthma.[27]

Immunotherapy

Subcutaneous immunotherapy (SCIT) for children with allergic rhinitis was shown to prevent the subsequent development of allergic asthma.[28] The long-term effects of SCIT were evaluated in a 10-year follow-up study on a cohort who received SCIT in a randomised study.[29] All patients had allergic rhinoconjunctivitis at baseline. The SCIT group showed statistically significant improvements in rhinoconjunctivitis symptoms compared to those receiving conventional treatments. Among the SCIT group, 16 of 64 developed asthma compared to 24 of 53 in the control group (25 versus 45 percent, odds ratio 0.4, 95% CI 0.2-0.9). Children with allergic rhinitis who received prolonged pharmacotherapy and have a strong family history of asthma can be considered for immunotherapy, especially when the parents/guardians are motivated and understand the risks and benefits of the treatment.

Conclusion & future directions

Although past experience reveals that avoidance of allergens alone cannot reverse the rising trend of allergic diseases, recent studies indicate that the induction of immune tolerance is the key to success. National Asthma and Allergy Plans have shown that the community burden and costs of allergy could be reduced by a concrete and pragmatic public health action plan. After the success of the Finnish Asthma Programme that resulted in several nationwide improvements in asthmatic outcomes, a more ambitious Finnish Allergy Programme is now underway with two main focuses: strengthening immune tolerance in early life; and early intervention in the course of allergic diseases.[30] The development of immune tolerance is related to sufficient exposures to environmental and commensal microbes in terms of diversity and quantity. Some practical strategies on allergy prevention and immune tolerance induction are summarised in the following table:

Strategies on allergy prevention and tolerance induction
Promote breastfeeding, no special diet for pregnant women and lactating mothers
Introduce complementary foods from 4-6 months of age
Stop cigarette smoking
Control air pollution and indoor air quality
Use of probiotics and other bacteria-containing (fermented) products
Consumption of fresh fruits and vegetables
Spending time in nature with outdoor physical activities
Weight control and avoid obesity
Avoid allergens only if necessary
Recognise and treat severe allergies early
Judicious use of antibiotics

Furthermore, the networking of specialists with primary care doctors, nurses and pharmacists is key to effective implementation, along with educational campaigns to increase allergy awareness and knowledge among patients and the general public. At a time when allergic individuals are already becoming the majority in urban populations with numbers continuously rising, it is time to collaborate and act proactively.

References

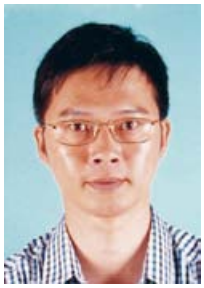
1. Pawankar R, Canonica GW, Holgate ST, Lockey RF. World Allergy Organization white book on allergy. World Allergy Organization (2013 update).
2. Eichenfield LF, Hanifin JM, Lemanske RF Jr, et al. Atopic Dermatitis and Asthma: Parallels in the Evolution of Treatment.Pediatrics 2003;111:608–16.
3. Zeiger RS. Food Allergen Avoidance in the Prevention of Food Allergy in Infants and Children.Pediatrics 2003;111:1662–71.
4. Fälth-Magnusson K, Kjellman NI. Development of Atopic Disease in Babies Whose Mothers Were Receiving Exclusion Diet during Pregnancy--a Randomized Study.J Allergy ClinImmunol 1987;80:868–75.
5. Section on Breastfeeding. Breastfeeding and the Use of Human Milk. Pediatrics 2012;129;e827–41.
6. Dogaru CM, Nyffenegger D, Pescatore AM, Spycher BD, Kuehni CE. Breastfeeding and Childhood Asthma: Systematic Review and Meta-Analysis.Am J Epidemiol 2014;179:1153–67.
7. Patel R, Oken E, Bogdanovich N, et al. Promotion of Breastfeeding Intervention Trial (PROBIT): A Randomized Trial in the Republic of Belarus.JAMA 2001;285:413–20.
8. Muraro A, Dreborg S, Halken S, et al. Dietary Prevention of Allergic Diseases in Infants and Small Children. Part III: Critical Review of Published Peer-Reviewed Observational and Interventional Studies and Final Recommendations.Pediatr Allergy Immunol 2004;15:291-307.
9. Mimouni Bloch A, Mimouni D, Mimouni M, Gdalevich M. Does Breastfeeding Protect against Allergic Rhinitis during Childhood? A Meta-Analysis of Prospective Studies.ActaPaediatr 2002;91:275-9.
10. Berg Av, Krämer U, Link E, et al. Impact of Early Feeding on Childhood Eczema: Development after Nutritional Intervention Compared with the Natural Course - the GINIplus Study up to the Age of 6 Years.ClinExp Allergy 2010;40:627-36.
11. Oldaeus G, Anjou K, Björkstén B, Moran JR, Kjellman NI. Extensively and Partially Hydrolysed Infant Formulas for Allergy Prophylaxis. Arch Dis Child 1997;77:4-10.
12. Zutavern A, Brockow I, Schaaf B, et al. Timing of Solid Food Introduction in Relation to Eczema, Asthma, Allergic Rhinitis, and Food and Inhalant Sensitization at the Age of 6 Years: Results from the Prospective Birth Cohort Study LISA. Pediatrics 2008;121:e44-52.
13. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). Scientific Opinion on the appropriate age for introduction of complementary feeding of infants. EFSA Journal 2009; 7(12): 1423.
14. Johnston M, Landers S, Noble L, Szucs K, Viehmann L. Breastfeeding and the Use of Human Milk, Pediatrics 2012;129(3):e827-41.
15. Roduit C, Frei R, Depner M, et al. Increased Food Diversity in the First Year of Life Is Inversely Associated with Allergic Diseases, J Allergy ClinImmunol 2014;133(4):1056-64.
16. Fleischer DM, Spergel JM, Assa'ad AH, Pongracic JA. Primary prevention of allergic disease through nutritional interventions, J Allergy ClinImmunolPract 2013;1(1):29-36.

17. Geuking MB, Cahenzli J, Lawson MA, et al. Intestinal Bacterial Colonization Induces Mutualistic Regulatory T Cell Responses, Immunity 2011;34(5):794-806.
18. Pelucchi C, Chatenoud L, Turati F, et al. Probiotics Supplementation during Pregnancy or Infancy for the Prevention of Atopic Dermatitis: A Meta-Analysis, Epidemiology 2012;23(3):402-14.
19. Fiocchi A, Pawankar R, Cuello-Garcia C, et al. World Allergy Organization-McMaster University Guidelines for Allergic Disease Prevention (GLAD-P): Probiotics, World Allergy OrganJ 2015;8(1):4.
20. Rao S, Srinivasjois R, Patole S, et al.Prebiotic Supplementation in Full-Term Neonates: A Systematic Review of Randomized Controlled Trials, Arch PediatrAdolesc Med 2009;163(8):755-64.
21. Mitchell EA, Beasley R, Keil U, et al. The Association between Tobacco and the Risk of Asthma, Rhinoconjunctivitis and Eczema in Children and Adolescents: Analyses from Phase Three of the ISAAC Programme, Thorax 2012;67(11):941-9.
22. Kalliola S, Pelkonen AS, Malmberg LP, et al.Maternal smoking affects lung function and airway inflammation in young children with multiple-trigger wheeze, J Allergy ClinImmunol 2013;131(3):730-5.
23. Guedes HT, Souza LS. Exposure to Maternal Smoking in the First Year of Life Interferes in Breast-Feeding Protective Effect against the Onset of Respiratory Allergy from Birth to 5 Yr, Pediatr Allergy Immunol 2009;20(1):30-4.
24. Mortimer K, Neugebauer R, Lurmann F, Alcorn S, Balmes J, Tager I. Air Pollution and Pulmonary Function in Asthmatic Children: Effects of Prenatal and Lifetime Exposures, Epidemiology. 2008;19(4):550-7.
25. Raciborski F, Tomaszewska A, Komorowski J, et al.The Relationship between Antibiotic Therapy in Early Childhood and the Symptoms of Allergy in Children Aged 6-8 Years - the Questionnaire Study Results, Int J Occup Med Environ Health2012;25(4):470-80.
26. Mitchell EA, Beasley R, Björkstén B, et al. The Association between BMI, Vigorous Physical Activity and Television Viewing and the Risk of Symptoms of Asthma, Rhinoconjunctivitis and Eczema in Children and Adolescents: ISAAC Phase Three, ClinExp Allergy 2013;43(1):73-84.
27. Maas T, Kaper J, Sheikh A, et al.Mono and Multifaceted Inhalant And/or Food Allergen Reduction Interventions for Preventing Asthma in Children at High Risk of Developing Asthma, Cochrane Database Syst Rev 2009;(3):CD006480.
28. Des Roches A, Paradis L, Menardo JL, Bouges S, Daurés JP, Bousquet J. Immunotherapy with a Standardized DermatophagoidesPteronyssinus Extract. VI. Specific Immunotherapy Prevents the Onset of New Sensitizations in Children, J Allergy ClinImmunol 1997;99(4):450-3.
29. Jacobsen L, Niggemann B, Dreborg S, et al. Specific Immunotherapy Has Long-Term Preventive Effect of Seasonal and Perennial Asthma: 10-Year Follow-up on the PAT Study, Allergy 2007;62(8):943-8.
30. Haahtela T, Valovirta E, Kauppi P, et al.The Finnish Allergy Programme 2008-2018 - Scientific Rationale and Practical Implementation, Asia Pac Allergy 2012;2(4):275-9.

Application of Component-resolved Diagnostics (CRD) in Food Allergy

Dr Marco HK HO
MBBS, MRCP, MRCPCH, FHKCpaed, FHKAM
Consultant, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital

Dr Eric YT CHAN
MBBS, FRCPath, FRCPA, FHKCPath, FHKAM
Consultant, Department of Pathology and Clinical Biochemistry, Queen Mary Hospital



Dr Marco HK HO Dr Eric YT CHAN

Introduction

Accurately diagnosing a patient with a possible food allergy is important to avoid unnecessary dietary restrictions and prevent life-threatening reactions. Routine testing modalities have limited accuracy, and an oral food challenge is often required to make a definitive diagnosis[1,2]. Given that they are labour intensive and associated with risks of inducing an allergic reaction, several alternative diagnostic tests have been investigated. Component-resolved diagnostics (CRD) is a diagnostic test to detect specific IgE against individual allergen molecules or components using purified native or recombinant allergens[3]. CRD has shown promise to improve diagnostics and has entered into clinical practice.

Advantages

One of the main advantages of CRD is to obtain information on the potential allergen cross-reactivity regarding inhalant allergens and food, which are exhibiting structural similarity within the epitopes. CRD explains at the molecular level allergens' cross-reactivity. It allows distinguishing cross-reactions that occur after ingestion of food in patients with hypersensitivity primarily to pollen from the coexistence of inhaled and food allergies. It is also possible to use CRD for selected allergens to predict the severity of allergic reactions that may follow ingestion of those specific food in patients with food allergy. In addition, in small children, CRD can be helpful in predicting the likelihood of developing tolerance to certain allergens. Finally, CRD is useful in identifying specific allergens for immunotherapy in allergic patients.

Technical aspects

Measurement of specific IgE against allergen components can only be performed by blood tests at present and there are singleplex or multiplex systems. In the former one component is tested per assay and the techniques are similar to those measuring sIgE to whole allergen extract. ImmunoCAP, CAP, radioallergosorbent test (RAST), sIgE and in vitro tests are common terms of this laboratory technique. Multiplex systems measure more than one component in each assay and there is one commercially available kit, the immune-solid phase allergen chip (ISAC) which has >100 allergen components from about 50 allergen sources coated on a biochip with several chips mounted on a slide.

Peanut

Not all peanut-sensitised children develop allergic reactions on exposure. In a population cohort, while 8-10 % children showed IgE sensitisation to peanut by skin test or food specific IgE measurement, only 1 in 5 of have clinical symptoms on challenge. The peanut component Ara h 2 was the most important predictor of clinical allergy.[4] A cut-off of Ara h 2 > 1.63 kU/l yielded a specificity of 100%, with a corresponding sensitivity of 70%. Symptom severity elicited during challenge correlated significantly with the levels of Ara h 2, but large individual variations were found[4]. This cut-off would have reduced the necessary number of oral challenges by half. This result was reproduced by another group which also found the outcome of the food challenge could be predicted with sIgE to Ara h 2 in 50% of the patients[5]. Using the same blood sample, a two-pronged blood test (with decision point at whole extract peanut IgE testing >15Kua/L and peanut Ara h2 >1 KUa /L) has reduced the need for oral food challenges four-fold in an Australian study[6].

Nonetheless, regional differences exist. In a study that compared patients with a peanut allergy from 3 countries (Spain, the United States, and Sweden), USA patients frequently had IgE against Ara h 1 to 3 that often manifested with severe symptoms, while sensitisation to Ara h 9 and Ara h 8 were primarily found in Spanish and Swedish patients, respectively[7].

Shrimp allergy

One study that included 37 adults presented the accuracy of a specific IgE antibody toward rPen a 1 for shrimp allergy[8]. Yang et al reported that sIgE antibodies to shrimp tropomyosin is more useful than a skin prick test to predict clinically relevant reactions in patients with shrimp allergy[9].

Egg allergy

A proportion of children with egg and milk allergies can tolerate cooked or the baked form of these foods. Such tolerance allows introduction of such foods and can greatly improve the ease of day to day management and quality of life of the patients and carers. However, a measurement of egg white-specific IgE levels has been shown to be a poor predictor of clinical phenotypes of egg allergy, including to raw egg white, but particularly to baked or cooked egg. Egg white and yolk contain

more than 20 different glycoproteins, including ovomucoid (Gal d 1), ovalbumin, ovotransferrin, alpha-livetin and the newly identified Gal d 6[10]. CRD helps to diagnose the different clinical phenotypes of egg allergy. An Italian study of egg allergy showed that 94% of Gal d 1 negative patients tolerated boiled egg; however, 95% of Gal d 1 positive patients reacted to raw egg[11]. Nevertheless in another study , sIgE against Gal d 1 has no better prediction than sIgE to egg white in assessing tolerance to baked egg[12].

Cow's milk allergy

Cow's milk protein allergens consist mainly of casein and whey proteins. The casein fraction (Bos d 8) accounts for 80% of total protein, while 20% is contained in whey proteins such as β-lactalbumin (Bos d 4), β-lactoglobulin (Bos d 5), bovine serum albumin (Bos d 6), immunoglobulin (Bos d 7), and lactoferrin[13]. Cingolani et al. used CRD to compare the levels of specific IgE against nBos d 4, nBos d 5, and nBos d 8 between the anaphylaxis group and non-anaphylaxis group of patients with CMA[14]. The level of IgE to nBos d 8 differentiated the "high anaphylaxis-risk" from the "milder-risk" group. However such results could not be consistently verified. Ott et al, evaluated the commercially available allergen microarray assay using Bos d 4, 5, 6, and 8 in patients with CMA[15]. They found that no single allergen component could discriminate asymptomatic sensitisation from clinically relevant allergy.

There have been more studies on diagnostic value of food allergies such as wheat, soybean, and hazelnut allergies[16-18].

Oral Allergy Syndrome (OAS)

OAS refers to a condition in patients who are sensitive to ragweed or birch pollens. When these patients eat certain fruits such as apples, cherries and melons they may rapidly develop an itchy, tingling sensation around the lips, with mild swelling. The tongue, palate and throat may also be involved. This is because the main allergen component in birch pollen, Bet v 1, is highly cross-reactive to many plant foods. For example, there is structural similarity between Bet v 1 and Ara h 8 in peanut or Cor a 1 in hazelnut. Fresh fruits, raw vegetables and nuts are common causes of OAS and the responsible allergen components are usually heat-labile. Hence cooked or processed forms of these foods are often tolerated.

Idiopathic anaphylaxis

A diagnosis of idiopathic anaphylaxis following a detailed clinical assessment remains very challenging if not frustrating for patients and clinicians. Risk reduction strategies such as allergen avoidance are not possible without knowledge of the culprit allergen. Heaps et al T using ISAC allergen array with 103 allergens investigated 110 patients with a diagnosis of idiopathic anaphylaxis from five UK specialist centres. The ISAC array contributed to the diagnosis in 20% of patients with idiopathic anaphylaxis. A wide range of major allergens were identified, the most frequent being omega-5-gliadin and shrimp. The authors suggested that it may offer additional information where a careful allergy history and follow-on testing have not revealed the cause of the anaphylaxis[19].

Clinical utility

We often refer to the usefulness and cost-effectiveness for any new test. Antonicelli et al found only fair agreement between allergists' risk assessment based on the current decision making process with that of allergen-oriented risk assessment through microarray-based immunoassay. Three main causes of discrepancy were the poor sensitivity of the allergen microarray-immunoassay, the differences in risk assessment established by the specialist and the microarray-immunoassay, and the non-inclusion of the causative allergen in the microarray-immunoassay platform.[20]

Allergy specialists want this test to be easy to use, easy to interpret and can reduce the need of oral challenge. In the current practice, CRD is an "add- on" test and it is not able to replace the whole extract igE testing. The additional cost could be partially offset by reducing the need of food challenge which could ease an overwhelmingly busy allergy health service. Thus cost effectiveness has to be assessed against different practice situations.

Limitation

CRD does not replace clinical observation and double-blind placebo-controlled food challenge, which is still the gold standard in the diagnosis of food allergy. Due to the geographic diversity in pollen exposure and dietary factors, researches on allergen components in populations living in different climatic zones give different results. CRD results should always be considered in the clinical context, especially when estimating the risk of severe allergic reactions. Practical conclusions and guidance derived from different populations should be drawn with caution.

Conclusion

Despite these limitations, the CRD method as a modern tool for the diagnosis of allergy deserves its increasing popularity. It provides information on allergenic components at the molecular level, allowing better understanding of the cause of symptoms and the introduction of individualised strategies for management. Validation for the local Hong Kong population is underway.

References

1. Sicherer SH, Sampson HA. Food allergy. J Allergy Clin Immunol 2010;125:S116-25.
2. Panel NI-SE, Boyce JA, Assa'ad A, et al Guidelines for the diagnosis and man¬agement of food allergy in the United States: report of the NIAID-sponsored expert panel. J Allergy Clin Immunol 2010;126:S1-58.
3. Treudler R, Simon JC. Overview of component resolved diagnos¬tics. Curr Allergy Asthma Rep 2013;13:110-7.
4. Eller E, Bindslev-Jensen C. Clinical value of component-resolved diagnostics in peanut-allergic patients. Allergy 2013;68:190-4.
5. Klemans RJ, Otte D, Knol M, et al. The diagnostic value of specific IgE to Ara h 2 to predict peanut allergy in children is comparable to a validated and updated diagnostic prediction model. J Allergy Clin Immunol 2013;131:157-63.

6. Dang TD, Tang M, Choo S, et al. Increasing the accuracy of peanut allergy diagnosis by using Ara h 2.J Allergy Clin Immunol. 2012;129(4):1056-63.
7. Vereda A, van Hage M, Ahlstedt S, et al. Peanut allergy: Clinical and immunologic differences among patients from 3 different geographic regions. J Allergy Clin Immunol 2011;127:603-7.
8. Ayuso R, Sánchez-Garcia S, Pascal M, et al. Is epitope recognition of shrimp aller¬gens useful to predict clinical reactivity? Clin Exp Allergy 2012;42:293-304.
9. Yang AC, Arruda LK, Santos AB, et al. Measurement of IgE antibodies to shrimp tropomyosin is superior to skin prick testing with commercial extract and measurement of IgE to shrimp for predicting clinically relevant allergic reactions after shrimp ingestion. J Al¬lergy Clin Immunol 2010;125:872-8.
10. Dang TD, Mills CE, Allen KJ. Determination of the clinical egg allergy phenotypes using component-resolved diagnostics. Pediatr Allergy Immunol. 2014 Nov 7. doi: 10.1111/pai.12301
11. Alessandri C, Zennaro D, Scala E, et al. Ovomucoid (Gal d 1) specific IgE detected by microarray system predict tolerability to boiled hen's egg and an increased risk to progress to multiple environmental allergen sen¬sitisation. Clin Exp Allergy 2012;42:441-50.
12. Bartnikas LM, Sheehan WJ, Larabee KS, Petty C, Schneider LC, Phipatanakul W. Ovomucoid Is Not Superior to Egg White Testing in Predicting Tolerance to Baked Egg. J Allergy Clin Immunol Pract 2013; 1:354-60
13. Restani P, Ballabio C, Di Lorenzo C, Tripodi S, Fiocchi A. Molecular aspects of milk allergens and their role in clinical events. Anal Bio anal Chem 2009;395:47-56.
14. Cingolani A, Di Pillo S, Cerasa M, et al. Usefulness of nBos d 4, 5 and nBos d 8 specific IgE antibodies in cow's milk allergic children. Allergy Asthma Immunol Res 2014;2:121-5.
15. Ott H, Baron JM, Heise R, et al. Clinical usefulness of microarray-based IgE detection in children with suspected food allergy. Allergy 2008;63:1521-8.
16. Pahr S, Constantin C, Papadopoulos NG, et al. J Allergy Clin Immunol 2013;132:1000-3.e1-4.
17. Ebisawa M, Brostedt P, Sjölander S, Sato S, Borres MP, Ito K. Gly m 2S albumin is a major allergen with a high diagnostic value in soy¬bean-allergic children. J Allergy Clin Immunol 2013;132:976-8.e1-5.
18. Masthoff LJ, Mattsson L, Zuidmeer-Jongejan L, et al. Sensitization to Cor a 9 and Cor a 14 is highly specific for a hazelnut allergy with objective symptoms in Dutch children and adults. J Allergy Clin Immunol 2013;132:393-9.
19. Heaps A, Carter S, Selwood C, et al. The utility of the ISAC allergen array in the investigation of idiopathic anaphylaxis. Clin Exp Immunol. 2014;177(2):483-90.
20. Antonicelli L, Massaccesi C, Braschi MC, Cinti B, Bilò MB, Bonifazi F.Component resolved diagnosis in real life: the risk assessment of food allergy using microarray-based immunoassay. Eur Ann Allergy Clin Immunol. 2014;46(1):30-4.

Management of Cow's Milk Protein Allergy

Ms June CHAN

MSc Exer & Nutr Sci Distinction (U Liverpool) BSC, Dietetics H. Hon (UC Davis), RD (USA), HKDA Accredited Dietitan

Senior Dietitian, Allergy Centre, Hong Kong Sanatorium & Hospital

Ms June CHAN

This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded 1 CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 31 May 2015.

Introduction

Cow's milk protein allergy (CMPA) is prevalent in the Western world and many Eastern countries, with a prevalence of 1.9-2.8% worldwide[1,2], and 2.3% in the China Mainland[3]. In Hong Kong, the estimated prevalence for CMPA from interview studies is 0.5%[4].

CMPA may be IgE-mediated and is indicated by a rapid onset of symptoms within 2 hours, or non-IgE mediated with delayed symptoms for up to weeks[5-7]. The diagnosis of IgE-mediated CMPA relies on a positive history of reaction towards ingestion of cow's milk with evidence of sensitisation; while non-IgE mediated CMPA requires elimination and reintroduction of cow's milk protein (CMP) correlated with symptoms occurrence to confirm. Lee et al has published a local guideline for diagnosis and treatment for CMPA in detail[8].

Once CMPA is diagnosed, dietary avoidance of CMP is warranted. Regular cow's milk and milk formulas, lactose free formulas, partially hydrolysed milk formulas and goat milk formulas are not suitable for patients with CMPA[2,9-15]. Recommendation on milk substitution is essential in older children, and is mandatory in children under 2 years old to ensure adequate calcium intake[15]. The best choice of milk substitute will be based on age, severity of CMPA, the presence of other food allergies and also the palatability of the formula. Assessment by a registered dietitian is preferable for education on milk avoidance, milk substitution and reintroduction, as well as assessment on growth and nutritional adequacy[2,15].

Milk Substitution

When a baby can be exclusively breastfed, breast milk should be advised. Maternal milk avoidance will be needed in exclusively breastfed infants with symptoms[15,16]. Infants 6 months or older receiving mostly breast milk should be given vitamin D supplementation[15].

Extensively hydrolysed formulas (EHF) can meet 90% clinical tolerance (with 95% confidence limits) in infants with proven CMPA[11,14,15]. In IgE-mediated CMPA children under 6 months with low risk of anaphylactic reactions, EHFs are the first treatment choice[2,14,15,17]. Infants reacting to breast milk may not be able to tolerate EHF[15].

Structurally, amino acid formulas are the most tolerable formulas for CMPA but often reserved due to their high cost and poor palatability. In children who are highly sensitised to CMP, such as those with IgE-mediated CMPA at high risk of anaphylaxis, severe non-IgE mediated CMPA including allergic eosinophilic oesophagitis, enteropathies, food protein-induced enterocolitis syndrome(FPIES), or exclusively breastfed infants with allergic symptoms, an amino acid formula is recommended[2,10,11,14,15,17].

Soy formulas are often used for infants with CMPA, but the following points must be taken into consideration before prescribing. About 10-14% of CMPA infants are sensitised to soy[7,14]. Similar to CMP, soy proteins have been strongly implicated in eosinophilic conditions of the gastrointestinal tract[7]. There have been concerns about the effect of soy formulas with its high phytoestrogen content[15]. Therefore, most guidelines do not recommend using soy formulas as milk substitutes in infants less than 6 months old[11,14,15,17]. Soy formulas can be considered in infants older than 6 months and without soy allergy.

Table 1. Cow's Milk Formula Substitution Available in Hong Kong for CMPA Infants

Formula Type	Brands
Extensively Hydrolysed Formula	Nutramigen Lipil (Mead Johnson) Alfare (Nestle) Nutrifant Pepti (Danone Nutricia) Pepti-Junior (Cow and Gate)
Amino Acid Formula	Neocate LCP (Nutricia SHS) Neocate Advance (Nutricia SHS)
Soy Formula	Nursoy (Wyeth) Isomil (Abbott)

Other non-dairy drinks with calcium

There is a great variety of non-dairy milk drinks including soy, almond, oat, and rice milk. While these beverages are free from CMP, they often have poorer nutritional values compared to infant formulas[15] and cow's milk[18], and should not be used for management of CMPA in infants. For children and adults, these drinks

can be used as substitutes with nutritional assessment and monitoring[15].

Reading food labels for a milk free diet

In order to avoid persistent symptoms, milk avoidance must be effective and complete. CMP is widely used in foods including pastries and snacks, making its avoidance very difficult and ingredient label reading essential. In addition, ensuring calcium intake from non-dairy sources is important. Consultation from a dietitian is helpful in ensuring the above and informing everyday choices[11].

Oral Immunotherapy

Oral immunotherapy (OIT) has opened a treatment option for CMPA with promising results[15]. Recent research showed that children have been treated with OIT are 5 to 10 times more likely to tolerate CMP compared to those on strict avoidance[19-21]. However, there are risks associated with OIT and precautions must be taken. Studies indicated adverse reactions, mostly mild to moderate, in one in every 6 doses[15]. At present, most guidelines do not recommend OIT for routine clinical practice[11,15,17,22].

Re-evaluation and reintroduction

Infants and children with CMPA should be re-evaluated every 2 to 4 weeks for their tolerance to the substitute-milk and every 6 to 12 monthly for their tolerance toward CMP[2,11,15]. Children who have developed clinical tolerance to cow's milk are suitable for reintroduction.

Baked milk products are tolerated by 75% of children with CMPA[23] as the high heat in the cooking process can reduce the allergenicity in CMP[6,14]. Therefore, milk reintroduction shall be started with baked foods containing small amounts of milk ingredients, such as crackers and biscuits[15,23]. Patients may then try foods with higher amounts of baked milk, then to milk less extensively cooked, and finally to boiled and fresh milk. A dietitian can provide personalised advice according to each patient's dietary habits.

Conclusion

CMPA is prevalent around the world. Once diagnosed, avoidance is warranted, and a substitute-milk shall be advised. Selection of the substitute-milk should be based on the patient's clinical tolerance and palatability of the substitute-milk. Education on food label reading is essential to achieve a total avoidance. OIT has opened a treatment option for CMPA but is not yet recommended for routine clinical practice. All CMPA patients should be re-evaluated and advised on milk reintroduction as appropriate.

References

1. Jakobsson, I. and T. Lindberg, *A prospective study of cow's milk protein intolerance in Swedish infants*. Acta Paediatr Scand, 1979. **68**(6): p. 853-9.
2. Boyce, J.A., et al., *Guidelines for the diagnosis and management of food allergy in the United States: summary of the NIAID-Sponsored Expert Panel Report*. Nutrition, 2011. **27**(2): p. 253-67.
3. Chen, J., et al., *The prevalence of food allergy in infants in Chongqing, China*. Pediatr Allergy Immunol, 2011. **22**(4): p. 356-60.
4. Ho, M.H., et al., *Prevalence of self-reported food allergy in Hong Kong children and teens--a population survey*. Asian Pac J Allergy Immunol, 2012. **30**(4): p. 275-84.
5. Ludman, S., N. Shah, and A.T. Fox, *Managing cows' milk allergy in children*. BMJ, 2013. **347**: p. f5424.
6. Eigenmann, J.M.J.A.W.B.M.P., *Food Allergy: Expert Consult Basic*. 1 ed. 2012: Elsevier Saunders.
7. Joneja, J.M.V., *The Health Professional's Guide to Food Allergies and Intolerances*. 1 ed. 2013: Academy of Nutrition and Dietetics.
8. Ho, M.H., J. Chan, and T.H. Lee, *Guideline for the diagnosis and management of cow's milk protein allergy CMPA) in Hong Kong* 2014, Hong Kong Institute of Allergy Hong Kong
9. Vandenplas, Y., et al., *Guidelines for the diagnosis and management of cow's milk protein allergy in infants*. Arch Dis Child, 2007. **92**(10): p. 902-8.
10. Kemp, A.S., et al., *Guidelines for the use of infant formulas to treat cows milk protein allergy: an Australian consensus panel opinion*. Med J Aust, 2008. **188**(2): p. 109-12.
11. Fiocchi, A., et al., *World Allergy Organization (WAO) Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) Guidelines*. PEDIATRIC ALLERGY AND IMMUNOLOGY, 2010. **21**: p. 1-125.
12. Surzhik, A.V. and T.E. Lavrova, *Review of international guidelines for the management of cow's milk protein allergy in infants, by using hypoallergenic formulas*. Rossiiskii Vestnik Perinatologii i Pediatrii, 2011. **56**(4): p. 104-108.
13. Lee, W.S., et al., *Malaysian Society of Allergy and Immunology and Malaysian Pediatric Association Guidelines for the management of cow's milk allergy in children 2012v*. 2012, Malaysian Society of Allergy and Immunology: Malaysia.
14. Koletzko, S., et al., *Diagnostic approach and management of cow's-milk protein allergy in infants and children: ESPGHAN GI Committee practical guidelines*. J Pediatr Gastroenterol Nutr, 2012. **55**(2): p. 221-9.
15. Luyt, D., et al., *BSACI guideline for the diagnosis and management of cow's milk allergy*. Clin Exp Allergy, 2014. **44**(5): p. 642-72.
16. Host, A., et al., *Bovine beta-lactoglobulin in human milk from atopic and non-atopic mothers. Relationship to maternal intake of homogenized and unhomogenized milk*. Clin Exp Allergy, 1990. **20**(4): p. 383-7.
17. Lee, S.K., A; Hamzah A; Chai, PF; Cheong, HK; Chong, SY; Kew, ST; Ng, RT, *Guidelines for the management of cow's milk allergy in children 2012v*, M.S.o.A.a.I.a.M.P. Association, Editor. 2012, Malaysian Society of Allergy and Immunology: Malaysia.
18. Lee, G.J., et al., *Consumption of non-cow's milk beverages and serum vitamin D levels in early childhood*. CMAJ, 2014. **186**(17): p. 1287-93.
19. Brozek, J.L., et al., *Oral immunotherapy for IgE-mediated cow's milk allergy: a systematic review and meta-analysis*. Clin Exp Allergy, 2012. **42**(3): p. 363-74.
20. Yeung, J.P., et al., *Oral immunotherapy for milk allergy*. Cochrane Database Syst Rev, 2012. **11**: p. CD009542.
21. Calatayud, C.M., et al., *Safety and efficacy profile and immunological changes associated with oral immunotherapy for IgE-mediated cow's milk allergy in children: systematic review and meta-analysis*. J Investig Allergol Clin Immunol, 2014. **24**(5): p. 298-307.
22. Venter, C., et al., *Diagnosis and management of non-IgE-mediated cow's milk allergy in infancy - a UK primary care practical guide*. Clin Transl Allergy, 2013. **3**(1): p. 23.
23. Nowak-Wegrzyn, A. and A. *Fiocchi, Rare, medium, or well done? The effect of heating and food matrix on food protein allergenicity*. Curr Opin Allergy Clin Immunol, 2009. **9**(3): p. 234-7.

MCHK CME Programme Self-assessment Questions

Please read the article entitled "Management of Cow's Milk Protein Allergy" by Ms June CHAN and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 31 May 2015. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please answer T (true) or F (false)

1. Once cow's milk protein allergy (CMPA) is diagnosed, dietary avoidance of cow's milk protein (CMP) is warranted.
2. Partially hydrolysed milk formulas and goat milk formulas can be considered for treatment of mild CMPA.
3. Maternal milk avoidance will be needed in all exclusively breastfed infants.
4. Extensively hydrolysed formulas can be tolerated by most CMPA infants.
5. Amino acid formulas are recommended for infants with IgE-mediated CMPA at high risk of anaphylaxis.
6. Soy formulas can be given to all infants older than 6 months.
7. Non-dairy milk drinks often have poorer nutritional values compared to cow's milk.
8. All children with CMP allergy should be desensitised by oral immunotherapy with milk.
9. Infants and children with CMPA should be re-evaluated every 6 to 12 months for their tolerance to the substitute-milk.
10. Milk reintroduction shall be started with baked foods such as crackers and biscuits.

ANSWER SHEET FOR MAY 2015

Please return the completed answer sheet to the Federation Secretariat on or before 31 May 2015 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Management of Cow's Milk Protein Allergy

Ms June CHAN

MSc Exer & Nutr Sci Distinction (U Liverpool) BSC, Dietetics H. Hon (UC Davis), RD (USA),
HKDA Accredited Dietitan

Senior Dietitian, Allergy Centre, Hong Kong Sanatorium & Hospital

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

Name (block letters):_____ HKMA No.: _____ CDSHK No.: _____

HKID No.: __ __ - __ __ __ __ X X (X) HKDU No.: _____ HKAM No.: _____

Contact Tel No.:_____ MCHK No.: _____ (for reference only)

Answers to April 2015 Issue

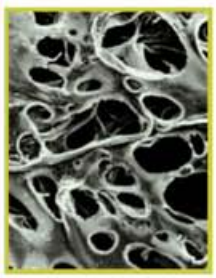
Multidisciplinary Refractory Epilepsy Evaluation Programme

1. T **2.** F **3.** T **4.** T **5.** T **6.** T **7.** T **8.** T **9.** T **10.** T

Discover th

Ecz

Imm
and



ImmunoCAP technology:
Excessive allergen componer
covalently bound to the high
ity, 3-dimensional cellulose p
to give reliable results.

Contact of ThermoFisher S
Hotline: 3192-7740
Fax: 2567-4447
Email: sales.hk@thermofis

More than a dozen of quality
ImmunoCAP blood testing, p

ImmunoCAP®
Is it allergy?

ne Connection between Allergy and

zema / Rhinitis / Asthma / Gastrointestinal symptoms

mmunoCAP blood testing helps you identify allergy triggers
l develop a management plan for improved patient well-being

nts are
capac-
olymer

Why ImmunoCAP

- Recognized as **Gold Standard** for *in vitro* IgE testing
- Published in over **4,000 medical journals**
- The only technology mentioned in Guidelines (CLSI, EAACI, NIH/ NIAID etc.)
- FDA cleared, CE-IVD marked
- Production is ISO 13485 & GMP certified
- Standardized to WHO IgE reference 75/502
- Sophisticated ImmunoCAP technology and fully automated system gives precise and accurate results: proven in extensive researches and external quality assessment programs (CAP, UKNeqas etc.)
- The broadest allergen coverage, including allergen components
- Over 3,000 laboratories worldwide are using ImmunoCAP
- **Dedicated to allergy testing**: Detailed information of every ImmunoCAP allergen can be found in our professional website:

thermoscientific.com/phadia

cientific Hong Kong Office:

sher.com

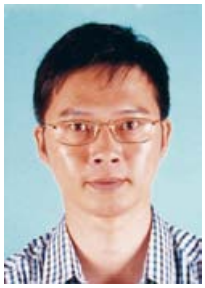
laboratories in Hong Kong are offering
lease contact us for further information.

ThermoFisher
SCIENTIFIC

Drug Allergy

Dr Eric YT CHAN
MBBS, FRCPath, FRCPA, FHKCPath, FHKAM
Consultant, Department of Pathology and Clinical Biochemistry, Queen Mary Hospital

Dr Marco HK HO
MBBS, MRCP, MRCPCH, FHKCpaed, FHKAM
Consultant, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital




Dr Eric YT CHAN Dr Marco HK HO

Introduction

Adverse drug reaction (ADR) includes all kinds of unexpected or undesirable effects of drugs and it concerns all clinicians across different disciplines. According to the latest USA national data, medications were the most common cause for fatal anaphylaxis attributing to close to 60% of all anaphylaxis deaths[1]. Drug hypersensitivity reaction (DHR) is one type of ADR clinically resembling allergy and if an immunologic mechanism can be defined it is referred to as Drug Allergy (DA). Guidelines and consensus statements were published on general or specific drug allergies[2,3]. The exact incidence of DA or DHR in Hong Kong is not known. In developed countries DHR is estimated to affect >7% of the general population and DA constitutes 5-10% of all ADRs[2,4]. Common drugs which give rise to DHR are antibiotics, non-steroidal anti-inflammatory drugs, anaesthetic agents, radio-contrast media. Risk factors of developing DA are female gender, previous allergic reactions to drugs, recurrent exposures to the same drug, HIV and other viral infections. Atopy by itself is not a risk of developing drug allergy but it may aggravate the severity of IgE-mediated drug reactions.

Classification and Pathophysiology

DHR can be classified into the immediate type and the non-immediate/ delayed type depending on the time interval between drug intake and onset of reaction. The immune mechanism responsible for the immediate type is IgE reaction (type I hypersensitivity), whereas the delayed type is the result of T-lymphocyte (type IV hypersensitivity), IgG and complement (type II hypersensitivity) or immune complex (type III hypersensitivity) actions. All types involve complex interactions of immune and non-immune cells resulting in typical clinical entities. Most drugs are small molecules and are non-immunogenic (haptens). They become antigens after binding to carrier proteins such as albumin. Antigen-presenting cells present the processed drug molecule in their HLA groove and B- and T-lymphocytes are activated. More recently an alternative theory, the pharmacological interaction with immune receptor (p-i) theory, emerges which states that drugs may in some cases directly bind to T cell receptors or HLA molecules resulting in T cell activation[5].

Clinical Features

Immediate DHRs occur usually <1 hour after taking the incriminating drug. Typical symptoms include:

1. Cutaneous: urticaria, angioedema
2. Respiratory: wheeze, rhinitis
3. Gastro-intestinal: nausea, vomiting, diarrhoea
4. Systemic: anaphylaxis

Non-immediate DHRs usually happen after 24 hours. They may present with:

1. Cutaneous: delayed urticaria, contact dermatitis, maculopapular rash, fixed drug eruptions, vasculitis, drug rash with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), acute generalised exanthematous pustulosis (AGEP)
2. Non-cutaneous: hepatitis, nephritis, pneumonitis, thrombocytopenia, neutropenia, anaemia.

Diagnosis

The proper time of investigation is 4-6 weeks after the complete resolution of signs and symptoms. Evaluation starts with a detailed clinical history and a thorough physical examination and is followed by specific procedures such as skin tests, in vitro tests and drug provocation tests.

Important questions in history taking are the drugs taken before the reaction, the time interval between drug intake and reaction onset, the clinical symptoms which are suggestive of drug allergy, any drug taken subsequently without problem and any similar reaction without taking the drug. A detailed examination of the skin is necessary as this is the organ most commonly involved in ADRs[6].

Skin tests are performed first by pricking the testing substance into the epidermis of the patient's skin (skin prick test). If the result is negative a more sensitive procedure is by injecting the testing drug into the dermis of the patient's skin (intradermal test). Both are read at 20 minutes (Figure 1) for immediate reactions and the intradermal results are also read at 48 hours for delayed reactions. For T-cell reactions, the patch test is an alternative procedure (Figure 2). The sensitivity of a patch test is lower than an intradermal test but it is more acceptable for severe reactions such as DRESS. Skin tests have been validated for the evaluation of immediate DHRs to beta-lactam antibiotics[7], neuromuscular blocking agents[8] and shown to have good sensitivity and specificity.

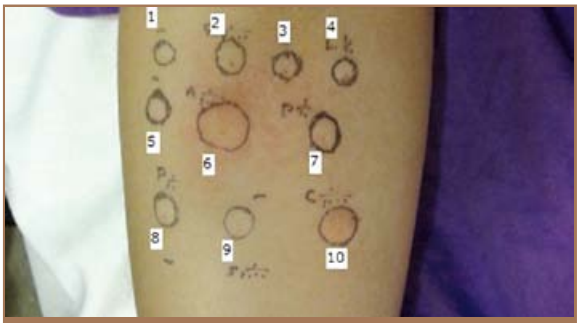


Figure 1 Intradermal skin test read at 20 minutes. Positive reactions to atracurium (6) and cis-atracurium (10). Negative reactions to saline control (1, 3, 5, 9), rocuronium (2), lidocaine (4), propofol (7, 8).

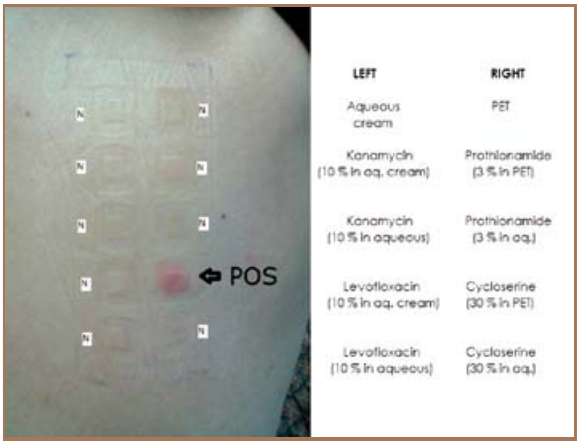


Figure 2 Patch test read at 48 hours. Positive reaction to cycloserine dissolved in petrolatum (arrow). Negative reactions to kanamycin, levofloxacin, prothionamide dissolved in aqueous cream or petrolatum or solvents only (N).

In vitro tests can measure drug-specific IgE in patients' serum or on patients' basophils by standardised laboratory procedures. Serum specific IgE tests are only available for a few drugs and the sensitivities are lower than skin tests though the specificities are equally good. Drug-specific T cells may be demonstrated by laboratory tests such as lymphocyte transformation or cytokine-release assays[9] but their availability is limited. In cases of anaphylaxis, a measurement of tryptase levels in blood is helpful in confirming the diagnosis[10]. Drug reactions to carbamazepine (CBZ) in Hans Chinese are strongly associated with HLA-B*15:02 and testing for this HLA allele is now mandatory[11]. A recent meta-analysis confirmed that in all populations, HLA-A*31:01 had an extremely strong association with CBZ-DRESS, but a much weaker association with CBZ-SJS/TEN[12]. SJS/TEN and possibly DRESS caused by allopurinol is associated with HLA-B*58:01.

Drug provocation tests (DPTs) are considered the gold standard in the diagnosis of DHRs and remain the only reliable method in evaluation of NSAID allergy[13]. To minimise other factors DPT is best carried out in a double-blinded placebo-controlled manner. These procedures are lengthy and risky and the benefits have to be balanced with the risks and the cost. Sometimes an open challenge is employed because the procedure is simpler though the result may be less accurate. All in vivo procedures, skin tests and DPT, must be carried out by experienced personnel in a medical setting with resuscitation facilities.

Treatment

Acute reactions should be managed promptly and all suspected drugs must be stopped immediately. If drug allergy is confirmed, it is generally recommended to avoid the drug and cross-reacting items lifelong. If an alternative drug is not available and treatment is necessary drug desensitisation can be attempted. It is defined as the induction of temporary tolerance by giving escalating doses starting with a small dose. There are published desensitisation protocols for some drugs, for example, allopurinol[14] and anti-lactam antibiotics[15]. For non-allergic DHRs, slow administration and pre-medications with anti-histamines and corticosteroids can help but these manoeuvres do not reliably prevent type I anaphylaxis.

Conclusions

Drug allergy is a common clinical problem and can have serious consequences. Given the high frequency of medication errors with resultant patient harm and cost, prevention is a worldwide priority for health systems. Systems that use information technology, such as computerised physician order entry, automated dispensing, barcode medication administration, electronic record reconciliation, and personal health record, are vital components of strategies to prevent drug hypersensitivity and errors; a growing body of evidence calls for their widespread implementation. Incorporate pharmacogenetic testing of certain HLA B loci before prescription helps to prevent severe drug hypersensitivity such as SJS/TEN and DRESS.

References

1. Jerschow E, Lin RY, Scaperotti MM, McGinn AP. Fatal anaphylaxis in the United States, 1999-2010: Temporal patterns and demographic associations J Allergy Clin Immunol. 2014;134(6):1318-1328.e7.
2. Demoly P, Adkinson NF, Brochow K et al. International consensus (ICON) on drug allergy. Allergy 2014; 69: 420-437.
3. Drug Allergy: An Updated Practice Parameter. Joint Task Force on Practice Parameters, representing the AAAAI, the ACAAI, and the Joint Council of Allergy, Asthma and Immunology. Ann Allergy Asthma Immunol 2010; 105: 259-273.
4. Anderson GA, Adkinson NF Jr. Allergic reactions to drugs and biological agents. JAMA 1987; 258: 2891-9.
5. Pichler WJ. The p-i concept: pharmacological interaction of drugs with immune receptors. World Allergy Organization Journal 2008; 1: 96-102.
6. Hausmann O, Schnyder B, Pichler WJ: Drug hypersensitivity reactions involving skin. Handb Exp Pharmacol 2010, 196:29–55.
7. Blanca M, Romano A, Torres MJ et al. Update on the evaluation of hypersensitivity reactions to betalactams. Allergy 2009: 64: 183–193.
8. Ebo DG, Fisher MM, Hagendorens MM, et al. Anaphylaxis during anaesthesia: diagnostic approach. Allergy 2007: 62: 471–487
9. Ebo DG, Leysen J, Mayorga C, et al. The in vitro diagnosis of drug allergy: status and Perspectives. Allergy 2011; 66: 1275–1286.
10. Schwartz LB. Diagnostic Value of Tryptase in Anaphylaxis and Mastocytosis. Immunol Allergy Clin N Am 2006; 26: 451–463.
11. Chen P, Lin J-J, Lu C-S. Carbamazepine-Induced Toxic Effects and HLA-B*1502 Screening in Taiwan. N Engl J Med 2011; 364:1126-1133.
12. Genin E, Chen DP, Hung SI, et al. HLA-A*31:01 and different types of carbamazepine-induced severe cutaneous adverse reactions: an international study and meta-analysis. Pharmacogenomics J. 2014 ;14(3):281-8.
13. Kowalski ML, Asero R, Bavbek S, et al. Classification and practical approach to the diagnosis and management of hypersensitivity to nonsteroidal anti-inflammatory drugs. Allergy 2013; 68: 1219–1232
14. Fam AG, Dunne SM, Lazzetta J, et al. Efficacy and Safety of Desensitization to Allopurinol following Cutaneous Reactions. Arthritis Rheum 2001; 44: 231-238.
15. Scherer K, Brockow K, Aberer W, et al. Desensitization in delayed drug hypersensitivity reactions – an EAACI position paper of the Drug Allergy Interest Group. Allergy 2013; 68: 844–852.

Leave allergy symptoms behind **for good** with **Neocate**

- Gold standard 100% amino acid-based formula
- Clinically proven rapid symptom relief regardless of complexity in 3-14 days[1,2]
- Clinically proven to improve growth in infants with CMA[3]
- New look and Advanced formulation
  - Macro & micro nutrient levels in line with the lastest guidlines[4,5,6]
  - The only AAF contains nucleotides
  - 1:1 DHA:ARA ratio for optimised inflammatory properties[7]

NEW LOOK
Advanced Formulation

Reference:
1. J. Pediatr 1997;131:744-747. 2.J Pediatr 1997 131:741-744. 3. Pediatr 1995;127:551-557

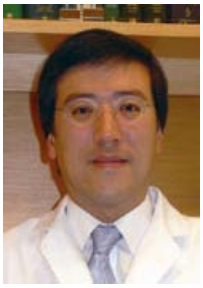
Further information is available upon request.
www.nutriciaclinical.com.hk
Hotline: 3460 5498

NUTRICIA
Neocate

Investigation and management of anaphylaxis

Dr Adrian WU

MB.,ChB, FRCP(Edin), FHKCP, FHKAM(Med), DABA&I
Specialist in Immunology and Allergy



Dr Adrian WU

Introduction

Anaphylaxis is defined as a "serious allergic reaction that is rapid in onset and can cause death."[1] It is one of the few true allergic emergencies and can be unpredictable and devastating. Therefore, all doctors who deal with patients should be familiar with the management of this condition.

Mechanisms

Anaphylaxis can be mediated by immune and non-immune mechanisms. The most common immune mechanism involves the binding of the allergen to specific IgE on the surface of mast cells and basophils, leading to degranulation and the immediate release of preformed and newly-formed mediators[2]. The common triggers of IgE-mediated anaphylactic reactions include food, drugs, insect stings, latex and environmental allergens such as pollens, dust and animal dander.

Mast cells also carry receptors for the complement products C3a and C5a, therefore complement activation can also lead to anaphylaxis[2]. This is usually triggered by antigen-IgG antibody complexes, but also through the activation of factor XII in the intrinsic coagulation pathway. Some agents can also cause direct mast cell degranulation, such as plasma expanders, radiocontrast media, opioids and muscle relaxants. Physical stimuli such as heat, cold and exercise can also trigger reactions in susceptible individuals through unknown mechanisms.

Symptoms during an anaphylactic reaction might include pruritis, skin rash, swelling, syncope, vomiting, abdominal cramps, diarrhoea, dyspnoea, wheezing and myocardial ischaemia/infarction. The onset of symptoms are usually from minutes to two hours after allergen exposure. A late-phase reaction might occur four to eight hours after exposure, after the acute symptoms have subsided.

Clinical Diagnosis

80% of patients present with cutaneous symptoms (urticaria and angioedema), but the lack of such symptoms does not exclude anaphylaxis. Important differential diagnoses to consider include acute asthma, vocal cord dysfunction, myocardial infarction, pulmonary embolism, vasovagal syncope, other forms of shock and psychiatric conditions.

It is important to identify the cause of the reactions. The clinical history is of paramount importance. Exposure to food, drugs, supplements and insect stings should be documented in detail. It is often necessary to refer to package labels and recipes for the ingredients. Dietary supplements may contain undeclared ingredients. Peanut, tree nut and shellfish allergens often trigger reactions within minutes after ingestion, whereas wheat allergens could trigger symptoms as late as 24 hours after exposure. Exercise, alcohol, heat and non-steroidal anti-inflammatory drugs could worsen allergic reactions; some patients would only react to food if one or more of these co-factors are present. The symptoms of scombroid fish poisoning are often indistinguishable from an allergic reaction. If other diners also suffer similar symptoms, it would suggest food poisoning.

The past medical history could be very helpful. Young children with a history of infantile eczema have an increased risk of food allergy. History of gastroesophageal reflux and/or colic could also suggest food allergy during infancy. Patients with pre-existing chronic urticaria are at increased risks of reacting to NSAIDs. Patients who are taking β-blockers or angiotensin converting enzyme inhibitors (ACEI) are at increased risks of severe anaphylaxis. Likewise, the mortality rate of anaphylaxis is increased in patients with pre-existing cardiovascular or pulmonary diseases. Moreover, ACEI can cause potentially fatal angioedema. The use of herbal supplements and medications should also be documented as allergic sensitivity to these products are not uncommon.

Allergic reactions can occur due to occupational exposure. It is therefore important to understand the patients' workplace environment and exposure.

Through the history, the physician should be able to identify possible triggers. The next step is to obtain evidence of the presence of allergen-specific IgE. Skin testing is a safe, fast and reliable means of confirming sensitisation. Anaphylactic reactions during skin testing have been documented, but these are very rare and are more commonly associated with testing for peanut, tree nuts or β-lactams. Facilities where skin tests are performed must be set up to deal with anaphylactic reactions. As there is a refractory period after an anaphylactic reaction, it is wise to wait three to four weeks before performing skin tests[3]. Specific IgE blood tests could also be used, but the reliability of the different tests available on the market can differ greatly. Only validated test methods approved by the FDA should be employed. There has been a proliferation

of blood tests for food-specific IgG in recent years. These tests are not FDA-approved, and have been shown to have no clinical utility in diagnosing allergy. Component testing could be useful in evaluating the risk of anaphylaxis in peanut allergy, as certain allergen components such as Ara h2 and Ara h6 are associated with increased risks of anaphylaxis.

Because of the low positive predictive value of allergy tests, we do not recommend indiscriminate "screening tests"[4]. Only items identified as likely candidates by the history should be tested. Clinical acumen is therefore very important in order to successfully identify the cause of these reactions.

Challenge testing remains the gold standard in allergy diagnosis. It is most frequently used in diagnosing reactions caused by physical stimuli, such as heat, cold, light, pressure, exercise and vibration. Graded oral challenge is sometimes required to diagnose certain drug allergies. Oral challenge should also be used to diagnose food allergy if the results of IgE/skin testing are in doubt, or to establish the threshold of reactivity[5].

Treatment

All patients at risk of anaphylaxis must carry self-injectable adrenaline, such as Epipen, Anapen or JEXT. The injections must be administered into the quadriceps muscle, because adrenaline given this way achieves high blood levels rapidly. Antihistamines and corticosteroids have a secondary role in the emergency treatment of anaphylaxis, but cannot replace adrenaline[6].

Allergen avoidance is still the mainstay in the prevention of anaphylaxis. However, some allergens are very difficult or impossible to avoid, such as insect stings, latex and environmental allergens. Under these circumstances, the patients should undergo allergen immunotherapy. Immunotherapy has been shown to be almost 100% effective in preventing insect sting anaphylaxis, and three to five years of treatment will provide life-long protection[7]. Immunotherapy could also be highly effective for certain food allergies and should be considered for patients who have difficulties in avoiding these foods[8-13]. Patients allergic to β-lactams, chemotherapeutic agents[14] or NSAIDs can likewise be desensitised prior to drug administration.

Patient education plays a most important role in managing anaphylaxis. Patients and their caregivers should be taught how to avoid exposure to allergens and situations that can lead to reactions. They should be aware of the common sources of cross-contamination in processed food and restaurant dishes. They must be familiar with the actions that need to be taken in case of an emergency. Schools should be informed and policies put in place to minimise risks. For example, in more and more states across the US, it is now mandatory for schools to keep unassigned self-injectable adrenaline. Unfortunately, most schools in Hong Kong still lack awareness of this problem, and efforts need to be made by the government and our medical community to address this issue.

Conclusion

Anaphylaxis is a potentially fatal condition with diverse causes involving different immunologic and non-immunologic mechanisms. The clinical history is the most important tool for diagnosis, supported by skin and laboratory testing. The first line of treatment is always adrenaline.

In many situations, avoidance is the only effective measure to prevent recurrence, and patient education is of paramount importance. Certain causes such as food, insect sting, latex, environmental allergens and drugs might be amenable to allergen immunotherapy.

References

1. Sampson HA, Munoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol 2006;117:391-7.
2. Peavy RD, Metcalfe DD. Understanding the mechanisms of anaphylaxis. Curr Opin Allergy Clin Immunol 2008;8:310-5.
3. Simons FER, Frew AJ, Ansotegui IJ, et al. Risk assessment in anaphylaxis: current and future approaches. J Allergy Clin Immunol 2007;120(suppl):S2-24.
4. Pereira B, Venter C, Grundy J, et. al. Prevalence of sensitization to food allergens, reported adverse reaction to foods, food avoidance, and food hypersensitivity among teenagers. J Allergy Clin Immunol 2005;116:884-92.
5. Nowak-Wegrzyn A, Assa'ad AH, Bahna SL, et al. Work group report: oral food challenge testing. J Allergy Clin Immunol 2009; 123(suppl):S365-83.
6. Alrasbi M, Sheikh A. Comparison of international guidelines for the emergency medical management of anaphylaxis. Allergy 2007;62:838-41.
7. Freeman TM. Clinical practice. Hypersensitivity to hymenoptera stings. N Engl J Med 2004;351:1978-84.
8. Burks AW, Laubach S, Jones SM. Oral tolerance, food allergy, and immunotherapy: implications for future treatment. J Allergy Clin Immunol 2008;121:1344-50.
9. Skripak JM, Nash SD, Rowley H, et al. A randomized, double-blind, placebo-controlled study of milk oral immunotherapy for cow's milk allergy. J Allergy Clin Immunol 2008;122:1154-60.
10. Longo G, Barbi E, Berti I, et al. Specific oral tolerance induction in children with very severe cow's milk-induced reactions. J Allergy Clin Immunol 2008;121:343-7.
11. Staden U, Rolinck-Werninghaus C, Brewe F, et al. Specific oral tolerance induction in food allergy in children: efficacy and clinical patterns of reaction. Allergy 2007;62:1261-9.
12. Jones SM, Pons L, Roberts JL, et al. Clinical efficacy and immune regulation with peanut oral immunotherapy. J Allergy Clin Immunol 2009;124:292-300.
13. Hofmann AM, Scurlock AM, Jones SM, P et al. Safety of a peanut oral immunotherapy protocol in children with peanut allergy. J Allergy Clin Immunol 2009;124:286-91
14. Castells MC, Tennant NM, Sloane DE, et al. Hypersensitivity reactions to chemotherapy: outcomes and safety of rapid desensitization in 413 cases. J Allergy Clin Immunol 2008;122:574-80.

PRINCESS CRUISES
come back new®

Japan 2015 DIAMOND PRINCESS®

9 Days Hokkaido Roundtrip Tokyo (Yokohama)

Tokyo (Yokohama), Japan | Kushiro, Japan |
Shiretoko Peninsula (Scenic Cruising), Japan | Korsakov, Russia | Otaru, Japan |
Hakodate, Japan | Aomori, Japan | Tokyo (Yokohama), Japan

July 8, 17 | August 19 **HK$10,990up** (CRUISE ONLY)

Taxes, Fees & Port Expenses approx: HK$772.19

Hirosaki Castle, Aomori

9 Days Northern Japan Roundtrip Tokyo (Yokohama)

Tokyo (Yokohama), Japan | Aomori, Japan | Akita, Japan |
Vladivostok, Russia | Hakodate, Japan | Tokyo (Yokohama), Japan

August 28 **HK$10,990up** (CRUISE ONLY)

Taxes, Fees & Port Expenses approx: HK$935.99

BEST CRUISE LINE IN ASIA
2014
WOMAN'S CHOICE AWARDS

Scan Here!!
For more 50th Celebration

Carnival Corporation Hong Kong Limited License No. 353772

Terms & Conditions applied, Princess Cruises reserves the right to add, edit, modify, delete any contents without giving any prior notice.

PRINCESS CRUISES
come back new®

2952 8088
www.princess.com

Suite 1207, Tower 1, The Gateway, Harbour City
25 Canton Road, Kowloon, Hong Kong

Wallball – Helping Children in Asia Stay Healthy & Become Olympic Champions

Mr Adrian LEE
Team GB Captain (2009-2012) & World Champion

Mr Adrian LEE

"Wallball." Say it again slowly, revelling in each syllable. "Wallball." It rolls off your tongue in a smooth, effortless way. Saying the word creates a pleasant sound that fills you with the same satisfaction as hitting a "roller", the shot that each wallballer craves whether they're playing socially in a friendly or in a winner-takes-all high stakes game.

Chances are you've not heard of wallball but you've probably found yourself playing a version of it during your childhood in those idle hours when all you had was a group of friends, a ball and some time to kill. The basic rules require players to strike a rubber ball with their hands against a wall and try to return it either on the volley or after a single bounce, similar to playing squash without a racquet.

The dimensions of the court are described on: http://ukwallball.co.uk/what-is-wallball/1-wall/ . The game can be played as both singles or doubles but there is no "tin" or bar against the front wall denoting the minimum height at which you must strike the wall. This means you can aim the ball as low as you want to try to win the point but obviously the lower you aim the higher the risk you will hit the floor before the wall and lose the point. The pinnacle of the game is hitting the aforementioned "roller", a shot that sends the ball hurtling to the bottom of the wall where it strikes the base and then rolls out along the floor in an un-returnable manner. Each roller creates the same reaction, a gasp of air followed by a thunderous, explosion of hooting and hollering by players and spectators alike. An audible appreciation of the skill involved in hitting one of these relatively rare shots that wins a point and ends a rally; a true art form in sport if ever you saw one.

Those who have played racquetball will be very aware of what the sport is like. You may even have seen it featured in a number of films over the years without realising what it was that people were playing. Recent memorable wallball scenes have appeared in Sleepers, Entourage and even in a Superbowl TV advert for Coca-Cola.

As a means of staying fit, wallball is one of the best activities available to someone wanting to lead an active and healthy lifestyle. As a means of developing coordination skills too it's unrivalled as players must learn to be ambidextrous, using either hand to strike the ball while sprinting back and forth and side to side to cover the court area. Studies have been conducted which place wallball above other renowned "lung-busters" such as squash, racquetball, running and swimming. At one point NASA astronauts were even required to take the game up as part of their fitness preparation for space missions! Despite these extreme health benefits, the beauty of the sport actually lies in the fact that players of all ages and levels are able to enjoy the game. At the World Championships held every three years, there are enormous numbers of juniors under ten years old as well as a surprisingly large number of elder statesmen and women over the age of seventy years playing. These tournaments happen in many different parts of the world with the U.S. and Ireland hosting the last two events and Canada hosting this year's competition.

The game originated in Ireland where different versions of the sport were played widely, traditionally 3-wall, 4-wall and more recently the 1-wall discipline available. Irish migrants then brought the sport over to the U.S. where the game experienced an explosion in uptake due to the abundance of players, space and the low cost of the game. All players need are a rubber ball, an existing wall and some chalk to mark out the court explaining why so many schools to this day have adopted the game for their students.

There are stories and old photos of wallball being played in the U.S. showing unemployed men passing the time and waiting for their roll-call for the next available job during the years of the Great Depression. The legacy of this cross-continent sporting jump across the pond is no more evident than in New York, the undoubted wallball Mecca and where every fan of the sport looks to visit either as a spectator or player. It's perhaps unsurprising then to discover that some of the top players both historically and currently playing the game have come from Stateside with the U.S., Puerto Rico, Mexico and Dominican Republic all providing exceptional players.

That being said, despite the undoubted dominance of players from the Americas, pockets of excellence are now appearing across other parts of the world, notably in Europe where the Pro-Wallball Tour has just been launched covering tournaments across multiple cities in an effort to centralise the game's rules and organisation. Top players from England, Ireland, Spain, the Netherlands, Belgium, France, Italy and many other countries will contest competitions across Europe with ranking points being awarded at each tournament. The end of the season will output a ranking ladder of the top players plying their trade in Europe.

Interestingly the last few years have seen a steady influx of top U.S. players entering European tournaments in an effort to test themselves against the game's rising stars as well as to help grow the game globally. In Asia, the main wallball countries are Australia and Japan where

the game is played avidly by some dedicated players who have fallen in love with and are eager to promote the sport. The game has also been played in Indonesia, Hong Kong and even as far out as Nepal.

The ultimate vision for the sport is to gain Olympic Games recognition and inclusion. While this requires a significant amount of organisational work, there are a number of committees now in place driving the agenda to make this a reality. One of the original barriers to this happening was around the sport's name as it was previously referred to as "handball" in many countries. There is unfortunately already a sport in the Olympics under this name and so to avoid confusion a move is underway to rebrand the sport as "wallball". Players for the most part seem happy to use the new moniker and to spread news of the Olympic vision to anyone showing interest in the game. Another barrier which has been overcome was that every country had its own version of a hand ball sport. Wallball played against a single front wall has now been adopted as the unified version and everyone is driving it forward to greater recognition.

One huge step towards Olympic status was the invitation for wallball to take part in the World Games last year in Colombia, which is the testing ground for sports looking to gain Olympic inclusion. The sport was received well by both organisers and spectators alike which was great news for all involved. The added exposure of the sport has also started creating some interest commercially with Red Bull and Nike now actively involved in sponsoring top US players and tournaments as well as ESPN covering some of the U.S. tournaments on live stream online TV.

As much as everyone is excited about the growth of the game at the elite-end of the player spectrum, there is also just as much excitement and effort going into promoting the sport among up-and-coming stars in schools. One of the most successful examples is the well established pilot programme in New York called "Inner City Handball" (ICH), that rolled wallball out to inner city schools to promote the sport among the next generation of athletes. Most importantly the sport helps to keep the children out of gangs and crime. The same principles were adopted by the UK Wallball association and they have now coached over 5,000 students in and around London.

My personal aim is to try and bring knowledge and increased participation of this amazing sport to those in Hong Kong and across Asia wherever I travel. Ideally, I would like to find a way to connect with those in positions of education and sport to identify how we can bring this low-cost game into schools and make it part of the sporting curriculum, either through scheduled day classes or in after school, extra-curricular opportunities. Having seen the huge benefits the game has brought to young children in other parts of the world, I have no doubt this sport will contribute in a big way to any school's offering it to its students as well as to local communities. Please do get in touch with me (AdrianTLLee@gmail.com) if you would like to find out more or if you would just like to try the sport. I'm happy to run a taster coaching clinic! You can also watch a teaser video explaining more about the game on http://youtu.be/kjmxQ-qH6gQ.

Dermatological Quiz

Dr Lai-yin CHONG
MBBS(HK), FRCP(Lond, Edin, Glasg), FHKCP, FHKAM(Med)
Specialist in Dermatology & Venereology

Dr Lai-yin CHONG

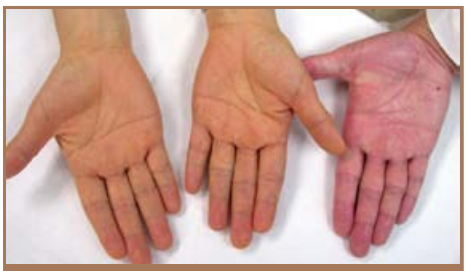


Fig.1: Yellowish discoloration of palms (versus a normal palm)

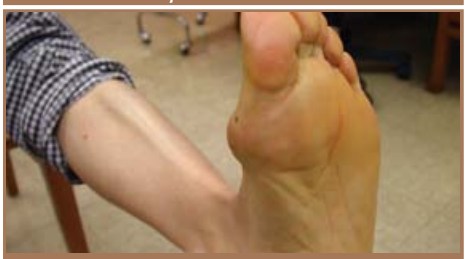


Fig.2: Yellowish discoloration at plantar area

This 14-year-old teenager had asymptomatic yellowish discoloration at both palms and soles. The colour progressively increased in the past six months. There were no tea-colour urine and no involvement of sclerae. Past health was otherwise good. His parents were worrying about liver disease in him.

Questions:

1. What are your diagnosis and the most important differential diagnosis?
2. What important information should you ask in the history?
3. What are the other medical causes of this condition?
4. How do you treat this patient?

(See P.36 for answers)

Medical Diary of May

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
					1	2
★ HKMA Table Tennis Tournament 2015 3	4	★ HKMA Yau Tsim Mong Community Network - The Journey to Optimize Type 2 Diabetes Therapy ★ FMSHK Officers' Meeting ★ HKMA Council Meeting 5	6	★ HKMA New Territories West Community Network - Certificate Course on Pain (Session 1) - Overview of Pain Management 7	★ HKMA Kowloon City Community Network - Latest COPD Management 8	★ Refresher Course for Health Care Providers 2014/2015 - Upper gastrointestinal update in primary care 9
10	★ HKMA CME - Comprehensive Management of Erectile Dysfunction: 1) Erectile Dysfunction Udpate - Cardiovascular Health Association and Oral Therapy 2) Non-medical Tratment of Erectile Dysfunction: Looking into the Future 11	★ HKMA Yau Tsim Mong Community Network - Sarcopenia Update ★ Inter-hospital Rheumatology Meeting 2015 12	★ HKMA Central, Western & Southern Community Network – Male LUTS: Beyond BPH Management ★ Hong Kong Neurosurgical Society Monthly Academic Meeting – Radiosurgery 13	★ HKMA Kowloon East Community Network: 1) New Concepts and Updates in Management of GERD 2) Update on Pharyngitis Management ★ HKMA Structed CME Programme with Hong Kong Sanatorium & Hospital Year 2015 – Rheumatic Diseases Presenting with Joint Pain 14	★ HKMA Hong Kong East Community Network – Certificate Course on Neurology (Session 3) – Epilepsy and Approach to LOC 15	16
★ HKMAPS 2nd Seasonal Photo Competition 2015 17	18	19	20	★ HKMA New Territories West Community Network – Certificate Course on Pain (Session 2) – Medications for Pain Management ★ KECN-HKCFP-UCH – Certificate Course for GPs 2015 (Session 2) – Common ENT Problems in the Community ★ FMSHK Executive Committee Meeting ★ FMSHK Council Meeting 21	22	23
24	25	26	27	★ HKMA Hong Kong East Community Network – Certificate Course on Neurology (Session 4) – Parkinsonism: First Encounter and Subsequent Management 28	★ HKMA Yau Tsim Mong Community Network – Male LUTS: Beyond BPH Management ★ 23rd Annual Scientific Congress 29	★ 23rd Annual Scientific Congress ★ Hong Kong Primary Care Conference 2015 30
★ 23rd Annual Scientific Congress ★ Hong Kong Primary Care Conference 2015 31						

Date / Time	Function	Enquiry / Remarks
3 SUN	**HKMA Table Tennis Tournament 2015** Organiser: The Hong Kong Medical Association; Chairman: Dr. KOO Hok Tin, Hilton; Venue: TBC	Mr. Ian KWA Tel: 2527 8285
5 TUE 1:00 PM	**HKMA Yau Tsim Mong Community Network - The Journey to Optimize Type 2 Diabetes Therapy** Organiser: HKMA Yau Tsim Mong Community Network; Chairman: Dr. LEUNG Wai Fung, Anders; Speaker: Dr. MAK Wai Han, Maria; Venue: Jade Ballroom, Level 2, Eaton, Hong Kong, 380 Nathan Road, Kowloon	Ms. Candice TONG Tel: 2527 8285
8:00 PM	**FMSHK Officers' Meeting** Organiser: The Federation of Medical Societies of Hong Kong; Venue: Gallop, 2/F, Hong Kong Jockey Club Club House, Shan Kwong Road, Happy Valley, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
8:00 PM	**HKMA Council Meeting** Organiser: The Hong Kong Medical Association; Chairman: Dr. SHIH Tai Cho, Louis; Venue: HKMA Head Office, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong	Ms. Christine WONG Tel: 2527 8285
7 THU 1:00 PM	**HKMA New Territories West Community Network - Certificate Course on Pain (Session 1) - Overview of Pain Management** Organiser: HKMA New Territories West Community Network; Chairman: Dr. CHEUNG Kwok Wai, Alvin; Speaker: Dr. CHAN Chi Wing, Timmy; Venue: G/F., Marina Club House Lobby, Gold Coast Yacht and Country Club, 1 Castle Peak Road, Castle Peak Bay, Hong Kong (黃金海岸鄉村俱樂部‧遊艇會會所大堂)	Miss Hana YEUNG Tel: 2527 8285 1 CME Point
8 FRI 1:00 PM	**HKMA Kowloon City Community Network - Latest COPD Management** Organiser: HKMA Kowloon City Community Network; Chairman: Dr. CHIN Chu Wah; Speaker: Dr. CHU Chung Ming; Venue: Dragon King Restaurant (龍皇酒家), Shop 1, 3/F, Whampoa Gourmet Place, Site 8, Whampoa Garden, Hung Hom	Ms. Candice TONG Tel: 2527 8285 1 CME Point
9 SAT 2:15 PM	**Refresher Course for Health Care Providers 2014/2015 - Upper gastrointestinal update in primary care** Organisers: Hong Kong Medical Association & HK College of Family Physicians & HA - Our Lady of Maryknoll Hospital; Speaker: Dr. CHEUNG Wing I; Venue: Training Room II, 1/F, OPD Block, Our Lady of Maryknoll Hospital, 118 Shatin Pass Road, Wong Tai Sin, Kowloon	Ms. Clara Tsang Tel: 2354 2440 2 CME Points
11 MON 1:00 PM	**HKMA CME - Comprehensive Management of Erectile Dysfunction: 1) Erectile Dysfunction Udpate - Cardiovascular Health Association and Oral Therapy 2) Non-medical Tratment of Erectile Dysfunction: Looking into the Future** Organiser: Hong Kong Medical Association; Speakers: Dr. HO Kwan Lun & Dr. WONG Ming Ho, Edmond; Venue: HKMA Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	HKMA CME Dept. Tel: 2527 8285 1 CME Point
12 TUE 1:00 PM	**HKMA Yau Tsim Mong Community Network - Sarcopenia Update** Organiser: HKMA Yau Tsim Mong Community Network; Chairman: Dr. LAM King Hei, Stanley; Speaker: Dr. LIU Kin Wah; Venue: Pearl Ballroom, Level 2, Eaton, Hong Kong, 380 Nathan Road, Kowloon	Ms. Candice TONG Tel: 2527 8285 1 CME Point
6:00 PM	**Inter-hospital Rheumatology Meeting 2015** Organiser: The Hong Kong Society of Rheumatology; Chairman: Dr CW YIM; Speaker: Dr CHAN Ching Man; Venue: Hospital Authority Headquarters, Room 206S	Dr. LEE Ka Lai Tel: 9229 4616 1 CME Point
13 WED 1:00 PM	**HKMA Central, Western & Southern Community Network – Male LUTS: Beyond BPH Management** Organiser: HKMA Central, Western & Southern Community Network; Chairman: Dr. YIK Ping Yin; Speaker: Dr. LEE Chan Wing, Francis; Venue: HKMA Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Dr. LEE Wing Yan, Michael Tel: 2595 6456 1.5 CME Points
7:30 PM	**Hong Kong Neurosurgical Society Monthly Academic Meeting – Radiosurgery** Organiser: Hong Kong Neurosurgical Society; Chairman: Dr CHEUNG Fung Ching; Speaker: Dr CHU Chi Ho, Alberto; Venue: M Block, Ground Floor, Lecture Theatre, Queen Elizabeth Hospital	Miss Hana YEUNG Tel: 2527 8285 1 CME Point
14 THU 1:00 PM	**HKMA Kowloon East Community Network: 1) New Concepts and Updates in Management of GERD 2) Update on Pharyngitis Management** Organiser: HKMA Kowloon East Community Network; Chairman: Dr. AU Ka Kui, Gary; Speakers: Dr. LI Tat Wing, Francis & Dr. TAI Kian Bun; Venue: Lei Garden Restaurant (利苑酒家), Shop No. L5-8, apm, No. 418 Kwun Tong Road, Kwun Tong	Miss Hana YEUNG Tel: 2527 8285 1 CME Point
2:00 PM	**HKMA Structed CME Programme with Hong Kong Sanatorium & Hospital Year 2015 – Rheumatic Diseases Presenting with Joint Pain** Organisers: Hong Kong Medical Association & Hong Kong Sanatorium & Hospital; Speaker: Dr. CHAN Ka Yan, Helen; Venue: HKMA Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	HKMA CME Dept. Tel: 2527 8285 1 CME Point
15 FRI 1:00 PM	**HKMA Hong Kong East Community Network – Certificate Course on Neurology (Session 3) – Epilepsy and Approach to LOC** Organiser: HKMA Hong Kong East Community Network; Chairman: Dr. GOH Kim Yeow; Speaker: Dr. LO Chi Hung; Venue: HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong	Ms. Candice TONG Tel: 2527 8285 1 CME Point
17 SUN 2:00 PM	**HKMAPS 2nd Seasonal Photo Competition 2015** Organiser: HKMA Photographic Society; Chairman: Dr. PANG Lai Man, Amy; Venue: HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong	Mr. Ian KWA Tel: 2527 8285
21 THU 1:00 PM	**HKMA New Territories West Community Network – Certificate Course on Pain (Session 2) – Medications for Pain Management** Organiser: HKMA New Territories West Community Network; Chairman: Dr. CHAN Lam Fung, Lambert; Speaker: Dr. CHAN Wing Sang; Venue: G/F., Marina Club House Lobby, Gold Coast Yacht and Country Club, 1 Castle Peak Road, Castle Peak Bay, Hong Kong (黃金海岸鄉村俱樂部‧遊艇會會所大堂)	Miss Hana YEUNG Tel: 2527 8285 1 CME Point
1:00 PM	**KECN-HKCFP-UCH – Certificate Course for GPs 2015 (Session 2) – Common ENT Problems in the Community** Organisers: HKMA Kowloon East Community Network & Hong Kong College of Family Physicians & United Christian Hospital; Chairman: Dr. MA Ping Kwan, Danny; Speaker: Dr. KWAN Man Yee, Wendy; Venue: V Cuisine, 6/F, Holiday Inn Express Hong Kong Kowloon East, 3 Tong Tak Street, Tseung Kwan O	Ms. Polly Tai / Ms. Cordy WONG Tel: 3949 3430 (Polly) / 3949 3087 (Cordy) Fax: 3949 5505 1 CME Point
7:00 PM	**FMSHK Executive Committee Meeting** Organiser: The Federation of Medical Societies of Hong Kong; Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898

Date / Time	Function	Enquiry / Remarks
21 THU 8:00 PM	**FMSHK Council Meeting** Organiser: The Federation of Medical Societies of Hong Kong; Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
28 THU 1:00 PM	**HKMA Hong Kong East Community Network – Certificate Course on Neurology (Session 4) – Parkinsonism: First Encounter and Subsequent Management** Organiser: HKMA Hong Kong East Community Network; Chairman: Dr. KONG Wing Ming, Henry; Speaker: Dr. TSANG Kin Lun; Venue: HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong	Ms. Candice TONG Tel: 2527 8285 1 CME Point
29 FRI 1:00 PM *(30, 31)*	**HKMA Yau Tsim Mong Community Network – Male LUTS: Beyond BPH Management** Organiser: HKMA Yau Tsim Mong Community Network; Chairman: Dr. LAM Siu Keung; Speaker: Dr. WONG Kwok Tin, Martin; Venue: Diamond Room V-Hall, Level B1, Eaton, Hong Kong, 380 Nathan Road, Kowloon **23rd Annual Scientific Congress** Organiser: Hong Kong College of Cardiology; Chariman: Dr CHIANG Chung Seung; Venue: Sheration Hong Kong Hotel & Towers	Ms. Candice TONG Tel: 2527 8285 1 CME Point Ms. Lynn LAM Tel: 2566 2889
30 SAT *(31)*	**Hong Kong Primary Care Conference 2015** Organiser: The Hong Kong College of Family Physicians; Venue: HKAM Jockey Club Building	Ms. Wing YEUNG / Ms. Carmen TONG Tel: 2528 6618 CME Points (Pending)

Certificate Course for General Public

Course No. C269 **CME/CNE Course**

Certificate Course on Off-Street Emergency Medicine

緊急情況下的急救治理證書課程

Jointly organised by

The Federation of Medical Societies of Hong Kong

Hong Kong Society for Emergency Medicine and Surgery

Date	Topics	Speakers
3 Jul	File 1 : An athletic injured in the sports field, the management and can he return to play? 運動員於運動場上受傷時的處理方法及是否可以繼續完成餘下的比賽？	Dr. Ken WU 胡永祥醫生 香港急症科醫學院院士
10 Jul	File 2 : A person you meet with shortness of breath, chest pain or dizziness during mountain trekking, what should I do? 如目睹行山人士呼吸困難、胸口痛楚及出現暈眩症狀，可怎樣提供協助?	Dr. Axel SIU 蕭粵中醫生 香港急症科醫學院院士
17 Jul	File 3 : A person collapsed in street, legal aspects and medical treatment. 如何提供適當及合法的醫療治理予在街上暈倒的途人。	Dr. Abraham WAI 衛家聰醫生 香港急症科醫學院院士
24 Jul	File 4 : A person knocked down by a car outside your clinic, can you help? 你可以怎樣協助因被車撞倒的傷者？	Dr. Fong-lun LEE 李方倫醫生 香港急症科醫學院院士
31 Jul	File 5 : A kid accidentally taken wild plants in the park, what can I do? 兒童在園內胡亂採摘野生植物而中毒，可怎樣處理？	Dr. Man-li TSE 謝萬里醫生 香港急症科醫學院院士
7 Aug	File 6 : A person bitten by animal, snake, dog, cat or stung by insect ? 怎樣適當地處理被動物、蛇、狗、貓咬傷或昆蟲刺傷？	Dr. Ralph CHEUNG 張冠豪醫生 香港急症科醫學院院士

Enquiry : The Secretariat of The Federation of Medical Societies of Hong Kong
Tel.: 2527 8898 Fax: 2865 0345 Email: info@fmshk.org

FMSHK 50th Anniversary Gala Dinner - "VIVA Federation!"

On 15 March 2015, the Federation of Medical Societies of Hong Kong held our 50th Anniversary Gala Dinner at the InterContinental Ballroom, Kowloon to celebrate this important milestone of the Federation. The Gala Dinner was indeed a most memorable event to our Federation, with our 137 member societies and over 50,000 strong professionals which we represent. The occasion has enhanced significantly the unity and fraternity of our member societies, friends and partners of our Federation.

With the theme "VIVA Federation!" the programme and venue were designed to match the joyous celebration atmosphere. Our President, Dr Raymond LO, delivered his welcome speech at the opening ceremony. We were most honoured to have the Patron of the Federation, the Chief Executive of Hong Kong SAR, The Honourable Mr CY LEUNG delivered the opening remarks. We were also privileged to have many distinguished guests joining us, including 國家衞生計生委家庭發展司巡視員 Ms Meilin XU; Secretary for Food and Health, Dr Wing–man KO; Under Secretary for Food and Health, Prof Sophia CHAN; Director of Health, Dr Constance CHAN; Chief Executive of the Hospital Authority, Dr Pak-yin LEUNG; Chairman of the Hospital Authority, Dr Che-yan LEONG; Chairman of the Council of the University of Hong Kong, Dr Che-hung LEONG; The Hon Dr Ka-lau LEUNG, The Prof Hon Joseph LEE and Prof Diana LEE together with past presidents of FMSHK, Dr Chok-wan CHAN & Dr Dawson FONG.

With the fabulous performing artists Joe Jr, Louie CASTRO, Suzan GUTERRES & Mimi LO, Alex LEE and Roger FUNG, the dinner was indeed a star-studded event with excellent entertainment. We were also delighted to have superb performances delivered by Dr David FANG & Dr York CHOW. To match with the theme, we established the "60s – 80s Fashion King & Queen Prizes". We appreciated all the participations from the chic & fashionable contestants, and congratulated all the winners of the contests & our grand raffles prizes.

A series of limited edition FMSHK 50th Anniversary souvenirs e.g. t-shirt, tie, bow tie & pin etc. are now available for purchase. Please visit our website for ordering.

We would like to express our sincere gratitude to all our sponsors and thank all our guests for joining us on this memorable occasion.


FMSHK 50th Anniversary Gala Dinner
FMSHK 50th Anniversary
THE FEDERATION OF MEDICAL SOCIETIES OF HONG KONG
FMSHK 50th Anniversary Gala Dinner


FMSHK 50th Anniversary
Logo Design Competition
THE FEDERATION OF MEDICAL SOCIETIES
FMSHK 50th Anniversary Gala
FMSHK 50th Anniversary Gala Dinner

Answers to Dermatological Quiz

1. Carotenoderma (Xanthoderma)
   This is the characteristic clinical feature of carotenemia due to increased beta-carotene levels in the blood. Carotene is a lipophilic lipochrome, which will deposit in the stratum corneum. The maximum accumulation occurs in areas with abundant sweat glands, such as the nasolabial folds, palms, and soles. This condition is more common in infants and children, clinically easily to be inspected in light-complexioned people and more pronounced under artificial light. In pigmented individuals, it may present mainly as yellowing of the palms and the soles. The most important differential diagnosis is jaundice, which can be easily excluded by the sparing of scleral involvement in carotenoderma. Other differential diagnoses include discoloration due to drugs or dye chemicals such as quinacrine (mepacrine), sorafenib, canthaxanthin, etc.

2. Dietary history
   Most of the cases are due to diet-induced carotenaemia following prolonged and excessive consumption of carotene-rich foods, such as carrots, oranges, squash, spinach, green beans, sweet potatoes, commercial infant food preparations, or carotene-rich nutritional supplements for vegetarians. As a rule of thumb, the deeper the yellow or green of a fruit or vegetable, the more carotene it contains. Lycopenaemia due to ingestion of large amounts of tomatoes or other fruits containing lycopene is considered as a variant of carotenaemia by some authors. On direct questioning, this patient had consumed large amounts of orange and orange juice daily to get Vitamin C, as his parents believed it will prevent him from flu.

3. Disease-related sources of carotenaemia include hypothyroidism, diabetes mellitus, anorexia nervosa, hepatic and renal disorders.

4. Carotenaemia is a benign condition which does not require specific treatment. Vitamin A toxicity does not occur as a result of such. Patients or parents of paediatric patients should be reassured and advised to consume a low-carotene diet, which will lead to gradual disappearance of the yellow skin discoloration over several weeks to months.

Dr Lai-yin CHONG
MBBS(HK), FRCP(Lond, Edin, Glasg), FHKCP, FHKAM(Med)
Specialist in Dermatology & Venereology

Nutrilon ProExpert HA

Prevention of the first allergy

ENP Early-life Nutritional Programming

For infants at risk of developing allergies due to FAMILY HISTORY

- ✓ Contribute to oral tolerance
- ✓ Reduce the risk of allergic manifestations

DOUBLE EFFECT

Partially hydrolysed formula

- Recommended for primary allergy prevention[1]
- Hypo-antigenic[2]
- Immune modulatory properties[3,4]

Prebiotics scGOS/lcFOS (9:1)

- Clinically proven to reduce the risk of allergic manifestations up to 5 years of age, including atopic dermatitis, recurrent wheezing, rhino conjunctivitis and urticaria[5,6]
- Reduce the risk of atopic dermatitis[7,8]
- Encourage a healthy gut microbiota[9]
- Help to naturally balance the immune system[10,11]

NUTRICIA®
Expert in Early-Life Nutrition

A complete portfolio from Immunity development to Allergy Prevention and Management

Immunity development

Allergy pervention

Allergy management

New packaging in March 2015

For infants without a family history of allergies

- Inspired by ENP Science
- Support Immunity, Metabolism and Brain development

For infants at risk of developing allergies due to family history

- Partially hydrolysed formula milk
- With a patented scGOS/lcFOS (9:1) mixture
- Clinically shown to contribute oral tolerance and reduce the risk of allergic manifestations

For infants with mild to moderate allergies

- Extensively hydrolysed formula milk
- With a patented scGOS/lcFOS (9:1) mixture
- Proven to relieve symptoms of CMPA

Reference: 8. Muraro, A., et al., EAACI food allergy and anaphylaxis guidelines.Primary prevention of food allergy. Allergy, 2014. 69(5): p. 590-601. 9. Tang, M., et al., Hypo-antigenic and immune modulatory properties of a partially hydrolyzed cow's milk formula supplemented with prebiotic oligosaccharides EAACI, 2014(Abstract number 1929). 10. van Esch, B.C., et al., In vivo and in vitro evaluation of the residual allergenicity of partially hydrolysed infant formulas. Toxicol Lett, 2011. 201(3): p. 264-9. 11. van Esch, B.C., et al., Interlaboratory evaluation of a cow's milk allergy mouse model to assess the allergenicity of hydrolysed cow's milk based infant formulas. Toxicol Lett, 2013. 220(1): p. 95-102. 12. Arslanoglu, S., et al., Early dietary intervention with a mixture of prebiotic oligosaccharides reduces the incidence of allergic manifestations and infections during the first two years of life. J Nutr, 2008. 138(6): p. 1091-5. 13. Arslanoglu, S., et al., Early neutral prebiotic oligosaccharide supplementation reduces the incidence of some allergic manifestations in the first 5 years of life. J Biol Regul Homeost Agents, 2012. 26(3 Suppl): p. 49-59. 14. Moro, G., et al., A mixture of prebiotic oligosaccharides reduces the incidence of atopic dermatitis during the first six months of age. Arch Dis Child, 2006. 91(10): p. 814-9. 15. Gruber, C., et al., Reduced occurrence of early atopic dermatitis because of immunoactive prebiotics among low-atopy-risk infants. J Allergy Clin Immunol, 2010. 126(4): p. 791-7. 16. Haarman, M. and J. Knol, Quantitative real-time PCR assays to identify and quantify fecal Bifidobacterium species in infants receiving a prebiotic infant formula. Appl Environ Microbiol, 2005. 71(5): p. 2318-24. 17. Martin, R., et al., Early life: gut microbiota and immune development in infancy. Benef Microbes, 2010. 1(4): p. 367-82. 18. Jeurink, P.V., et al., Human milk: a source of more life than we imagine. Benef Microbes, 2013. 4(1): p. 17-30.

Vannair™ pMDI

budesonide/formoterol

AstraZeneca
阿斯利康

Help your COPD patients do more

COPD

Vannair pMDI (budesonide/formoterol)

- **significantly improves lung function in 5 minutes[1, 2]**
- **shows faster onset of bronchodilation than salmeterol/fluticasone[1]**
- **makes a significant improvement in breathing[2]**
- **effectively prolongs time to exacerbation[2]**
- **eases bronchoconstriction and controls inflammation[3]**

COPD = chronic obstructive pulmonary disease pMDI = pressurized metered-dose inhaler.

Presentation: Budesonide/formoterol fumarate dihydrate pressurised inhalation suspension for oral inhalation (pMDI). **Indication: Asthma** – regular treatment of asthma where use of a combination (inhaled corticosteroid and long-acting β2-agonist (LABA)) is appropriate in adults and adolescents. **Chronic obstructive pulmonary disease (COPD)** – symptomatic treatment of moderate to severe COPD in adults with frequent symptoms despite long-acting bronchodilator use, and/or a history of recurrent exacerbations. Vannair is not indicated for the initiation of bronchodilator therapy in COPD. **Dosage: Asthma** – Dosage should be individualised according to disease severity. Dose should be titrated to the lowest when asthma is under control. **Vannair 80/4.5 μg & 160/4.5 μg/ dose pMDI:** Adults and adolescents (≥ 12yrs): 2 inhalations twice daily. Max 4 inhalations (2 inhalations twice daily). **COPD - Vannair 160/4.5 μg/ dose pMDI** Adults: 2 inhalations twice daily. Max. 4 inhalations (2 inhalations twice daily). **Contraindications:** Hypersensitivity to budesonide, formoterol or to one of the excipients. **Precautions:** Long-term use only applied in patients whose asthma cannot be adequately controlled on asthma controller medications and for the shortest duration of time required to achieve control of asthma symptoms. Separate rapid-acting bronchodilator must be available for rescue at all times. Not initiate for treating a severe exacerbation. Oral corticosteroid usage. Potential systemic effects of inhaled corticosteroids; infections / tuberculosis. Patients with increased susceptibility to sympathomimetic amines. Patients with pre-existing cardiovascular conditions, diabetes mellitus, hypokalaemia (particularly patients receiving digoxin). Children <12 yr. Pregnancy & lactation. **Interactions:** CYP3A4 inhibitors (eg ketoconazole); β receptor blocking agents (non-selective); other sympathomimetic agents; xanthine derivatives, mineralocorticosteroid and diuretics; Monoamine oxidase inhibitors, tricyclic antidepressants, quinidine, disopyramide, procainamide, phenothiazines, and antihistamines. **Undesirable effects:** Palpitations, Candida infections in the oropharynx; headache; tremor; mild irritation in the throat; coughing, hoarseness. **Full local prescribing information is available upon request. API.HK.UAN.0231**

Please contact (852) 2420-7388 or HKPatientSafety@astrazeneca.com for adverse drug reactions (ADR) reporting to AZHK

References
1. Lindberg S et al. Respirology 2007;12:732-739.
2. Rennard S et al. Drugs 2009;69(5):549-565.
3. Vannair Hong Kong Packaging Insert Mar 2011.

284705.022 29/11/2011