

Reports on Scientific Meetings

Hong Kong Dermatology Symposium 2016 and Atopic Dermatitis Symposium

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explained by the hairless mice model, which demonstrated that topical corticosteroids cause epidermal barrier functional defect and induced a keratinocyte-initiated inflammatory response. Moreover, alteration in skin microbiota is associated with changes in inflammatory response.

Adult atopic dermatitis and occupational hand eczema

Speaker: Eric CC Lan

Department of Dermatology, Kaohsiung Medical University, Taiwan

Atopic dermatitis (AD) is a common disease in adult population. Studies from Taiwan and Japan demonstrated that the prevalence of AD in adult population is 8% and 6.9% respectively according to physician diagnosis, while questionnaires for identifying AD showed its prevalence in adults to be 3.7% and 2.5% respectively. For the treatment of adult AD, topical corticosteroid is commonly used. One of the most frequently seen problems is topical corticosteroid withdrawal dermatitis. It is characterised by the onset of a more severe or diverse manifestation of AD after the withdrawal of topical corticosteroids. The cause may be

Occupational hand eczema is often noted in workers exposed to wet work. The development of hand eczema in adults is often assumed to be linked with the atopic status. In the Taiwanese study, it was demonstrated that although AD is the most important factor for developing hand eczema in nursing staff, only 17% of them have AD. However frequent hand washing with water is found to be the most significant behavioural risk factor associated with the development of hand eczema.

Learning points:

Adult AD is a common disease. One of the factors associated with occupational hand eczema is frequency of hand washing with water.

Genetics in atopic dermatitis

Speaker: Wen-hung Chung
Department of Dermatology, Chang Gung Memorial Hospital, Taiwan

Atopic dermatitis (AD) is an inflammatory skin disease associated with genetic and environmental factors. Genetics, epidermal barrier function of the skin and autoimmunity are all related to AD.

Filaggrin is a key component of the epidermal differentiation complex of stratum corneum. Filaggrin mutation study among different populations showed that it is associated with increased risk of atopic sensitisation of allergic rhinitis and asthma. Whole genome sequencing of AD reveals multiple molecular pathways and mechanisms involved in AD. There are three main groups of genetic variants, including genes related to: 1) epithelial function, e.g. FLG, FLG2, SPINK5, SPRR3 etc.; 2) adaptive immunity, e.g. IL18 RAP, IL12, IL4, IL31, IL17A etc.; 3) innate immunity, e.g. TLR2, TLR4, TLR9 etc.

Advanced genetic studies can enhance the ability to identify potential gene mutations related to severe AD, thus provide novel insights to the genetic basis and management strategies for the management for AD.

Learning points:

AD is associated with both genetic and environmental factors. The three main groups of genetic variants in AD include genes related to: 1) epithelial function, 2) adaptive immunity and 3) innate immunity.

Diabetic foot ulcer – a podiatrist perspective

Speaker: Sarah PS Tse
Department of Podiatry, Kwong Wah Hospital, Hong Kong

Diabetic foot ulceration (DFU) is a common complication of diabetes mellitus (DM) worldwide. The main causes include peripheral neuropathy, peripheral vascular disease and trauma. DM foot risk categorisation helps to determine treatment approach and to predict prognosis. The podiatrist plays an important role in the prevention and management of DFU. Podiatry input is essential for the early detection of vascular and neurological deterioration, biomechanical assessment, appropriate patient education programmes, provision of sharp debridement and wound management, and use of special wound dressings. Optimal care from a multidisciplinary team for DFU, including the assessment of adequate arterial blood supply for healing, assessment of neuropathy, diagnosis and treatment of infection are vital for the prevention and treatment of DFU. Patient education and empowerment are also part of the prevention and management goals.

Learning points:

Optimal care from a multidisciplinary team, including the podiatrist is vital for prevention and treatment of DFU.

Update on human papillomavirus (HPV)

Speaker: Paul KS Chan
Department of Microbiology, The Chinese University of Hong Kong, Hong Kong

There are about 200 types of human papillomavirus (HPV) identified to date. Human papillomavirus infects keratinocytes and causes cutaneous and mucosal lesions, including genital and oral lesions. A survey conducted in

Hong Kong showed that about one in ten adult women (21-45 years old) carry HPV in the cervix. Risk factors for HPV include greater lifetime number of sexual partners and smoking. Transmission and acquisition of HPV is mainly through sexual contact and mother to newborn (vertical transmission). Fomites may also play a role as the virus is quite resistant to disinfection. It can cause cervical cancer and cancer of anus, vagina, vulva and penis. It is also associated with oropharyngeal cancer. With improved screening tools and the availability of prophylactic vaccines, the incidence of cervical cancer is expected to decrease in countries that can afford these preventative strategies. However, the overall incidence of oropharyngeal cancers, which have been shown to be associated with HPV, is on a rising trend. Currently, there are three types of HPV vaccine available, including the bivalent, quadrivalent and 9-valent vaccines.

Learning points:

HPV can cause cervical cancer and other cancers including oropharyngeal cancer. There are three types of HPV vaccine available currently.

Staphylococcus in eczema: friends or foes

Speaker: Ellis KL Hon

Department of Paediatrics, the Chinese University of Hong Kong, Hong Kong

Atopic dermatitis is a common chronic relapsing dermatological disease. Atopic dermatitis is present in about 15% of children. Colonisation or infection by *Staphylococcal aureus* (SA) is believed to be an important factor in the pathophysiology of atopic dermatitis. Acute exacerbation or severe form of atopic dermatitis may be related to staphylococcal colonisation or infection. Treatment of staphylococcal colonisation or infection may result in improvement of quality of life and disease

control. *Methicillin-resistant staphylococcal aureus* infection is uncommon in patients with atopic dermatitis. Cloxacillin is the drug of choice in treatment of SA infection. However, anti-staphylococcal drugs and antiseptic agents are not the mainstay of treatment even for moderate to severe atopic dermatitis. There is no evidence on the benefit of oral or topical antibiotics in non-infected atopic dermatitis, and the clinical effects of antibiotics on infected atopic dermatitis are likely to be transient. Further research is required to study the use of antibiotics and antiseptics for reducing disease severity.

Staphylococcus epidermidis is often considered to be a commensal bystander in the skin microbiota. *Staphylococcus epidermidis* strain JK16 inhibits biofilm formation by SA, and it was believed that this inhibitory strain may have a role in the pathophysiology of atopic dermatitis and the organism may be associated with more severe form of disease.

Learning points:

Staphylococcus aureus is implicated in the pathophysiology of atopic dermatitis. The role of *Staphylococcus epidermidis* has to be explored by further studies.

Prevention of atopic dermatitis: an evidence based review

Speaker: Dominic YK Lai

Private Practice, Hong Kong

There is currently conflicting evidence in primary prevention of atopic dermatitis in high risk children. Dr. Lai presented the current evidence of different measures in prevention of atopic dermatitis.

It was demonstrated that daily use of emollient since birth in high risk newborns may prevent the development of atopic dermatitis. Exclusive

breastfeeding for at least six months may reduce the risk of developing atopic dermatitis in high risk infants who have family history of atopy. There is limited evidence that prolonged feeding with a hydrolysed formula compared to a cow's milk formula may reduce infant and childhood allergy. Antigen avoidance diet in a high-risk woman during pregnancy or lactation is unlikely to reduce her risk of giving birth to an atopic child and may pose a risk of maternal or fetal nutritional deficiency. The evidence of probiotics in prevention of atopic dermatitis is still unclear. The efficacy of probiotics may depend on the timing, dose and specific probiotic used. The role of vitamin D in prevention of atopic dermatitis is still controversial.

Learning points:

Primary prevention of atopic dermatitis in high risk children remains a controversial issue. Further randomised control trials are required to determine measures that prevent atopic dermatitis.

Update in management of atopic dermatitis

Speaker: Yoke-chin Giam
National Skin Centre, Singapore

Atopic dermatitis is the most common skin disease in childhood and runs a chronic relapsing course. Barrier dysfunction, skin inflammation and immune dysregulation play a role in the pathogenesis of atopic dermatitis. Genetic studies of atopic dermatitis have been performed concerning skin barrier dysfunction including filaggrin gene mutation, which leads to an early onset and more severe phenotype. More genes on skin barrier, innate and adaptive immune systems have been found to have an association with atopic dermatitis and may give rise to multiple phenotypes. The advancement of genetic research may result in a new molecular taxonomy of atopic dermatitis.

Compared to adults, treatment of paediatric atopic dermatitis is different. Individual countries have developed their own guidelines. In general, these standard guidelines have been effective on management of atopic dermatitis regarding to different severity. The use of proactive topical calcineurin inhibitors for subclinical inflammation in long term management of atopic dermatitis are currently preferred in some places. Newer emollients contain ceramides which help barrier repair and reduce transepidermal water loss. These represent a safe and useful adjunct in the treatment of childhood atopic dermatitis. It is also proposed that earlier use of emollients during neonatal period in babies at risk may have a preventive effect. Newer drugs include dupilumab, an interleukin-4 inhibitor, and topical phosphodiesterase-4 inhibitor. Alternative options like immunotherapy, probiotics, prebiotics and vitamin D lack convincing evidence in treatment of atopic dermatitis. Lastly, the psychosocial impact of childhood atopic dermatitis should not be overlooked during the management of atopic dermatitis.

Learning points:

More genes have been found to have an association with atopic dermatitis. Newer drugs include ceramide-containing emollients, biologics, and topical phosphodiesterase inhibitors.

Food allergies in atopic dermatitis – evaluation and management

Speaker: Mark Koh
Dermatology Service, KK Women's and Children's Hospital, Singapore

Food allergy has been reported in some children with atopic dermatitis, which can be IgE or non-IgE mediated. Risk factors include young age

(<2 years), moderate to severe atopic dermatitis, early onset eczema (before 3 to 6 months). In Hong Kong, studies showed that egg yolk, egg white are the most common food items leading to sensitisation, followed by shrimp, peanuts, crab and lobster.

Indications for investigating suspected food allergies in children with atopic dermatitis include immediate reaction to single foods, moderate to severe atopic dermatitis despite optimal treatment (especially in young infants and children <2 years), failure to thrive, presence of GI symptoms, repeated delayed reactions, change in behaviour, and before introduction of variety of foods.

Common investigations include the skin prick test and serum specific IgE levels. Others include atopy patch test, basophil activation test and the gold standard diagnostic test is oral food challenge test. Skin prick test provides a cheap and convenient way for detecting IgE-mediated allergy. It can give instant results. However it cannot distinguish between sensitisation and true allergy. It is not useful in non-IgE mediated allergies, drug allergies and dermatographism. It gives a high negative predictive value. Positive result requires clinical correlation unless a large wheal (mean diameter >7 mm) is seen.

Specific IgE assays have similar sensitivity and specificity to the skin prick test but are expensive and the result is not immediately available. It is preferred over the skin prick test in dermatographism, extensive skin disease and inability to stop antihistamine. However, a positive test only indicates sensitisation rather than allergy. False positive results can occur in patients with a high total IgE. Higher antibody level predicts a higher chance of symptoms on exposure of the allergen.

Management of food allergy includes avoidance of allergic foods, prescription of antihistamine and EpiPen (epinephrine) injection for type 1 reaction, multi-disciplinary eczema-allergy clinic assessment and desensitisation. Maternal

dietary avoidance has not been shown to have a protective effect on atopic dermatitis.

Learning points:

Moderate to severe atopic dermatitis despite optimal treatment especially under two years old should be considered for investigation of food allergy.

Mohs micrographic surgery in the periocular region

Speaker: Kelvin KL Chong

Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong

Basal cell carcinoma and sebaceous gland carcinoma are the most common skin cancers in the periocular region. Traditional excision using arbitrary surgical margins does not allow for tissue-sparing, and excision of tumours close to the medial canthus may result in lacrimal outflow injury.

Mohs micrographic surgery (MMS), also known as chemosurgery, was developed in 1930s by a US surgeon, Dr Frederic E. Mohs. It requires close collaboration between the dermatopathologist, surgeon and an experienced cryosection technician. It can achieve the maximum tissue preservation with clinical margins of less than 1 mm. However it has higher requirements in terms of time, medical staff involved and resources. Also, training for Mohs surgery is not available in Hong Kong.

The speaker and his team recently proposed a multidisciplinary model with a standardised protocol to achieve the merit of MMS in a team manner. They streamlined the cryosection procedure and achieved a significantly shorter turnover time for each level of Mohs removal, which was comparable or probably shorter to the standard frozen section technique.

Twenty patients with biopsy-proven BCC were successfully treated under the protocol. No local recurrence was seen after a mean duration of follow up for 60 months.

Learning points:

MMS is a safe and effective treatment for periocular skin malignancy.

What's new in paediatric dermatology?

Speaker: Yoke-chin Giam

Department of Paediatric Dermatology, National Skin Centre, Singapore

The following entities were discussed:

Enterovirus 71 and Coxsackie A6 are the most common enteroviruses affecting Chinese children in Singapore. Coxsackie A6 infection may cause atypical HFMD with a more severe presentation, high fever, atypical rash distribution and post-illness onychomadesis.

Symptoms and signs for suspected Zika virus infection include fever and maculopapular rash, and any of arthralgia, myalgia, headache and conjunctivitis. Mothers with Zika virus infection during pregnancy may give birth to infants with microcephaly. Testing is advised for symptomatic pregnant women, or asymptomatic pregnant women with a history of sexual exposure to an infected male partner. Testing with a 5 ml urine sample is preferred.

When annular urticaria (urticaria multiforme) is compared with erythema multiforme, the former is more commonly triggered by a viral illness or medications. It has shorter duration (<24-48 hours). Pruritus, limb or mucosal oedema may be present.

Increased trans-epidermal water loss in early infancy may indicate a risk of atopic dermatitis

(AD) later on. Early emollient use (within 3 weeks to 6 months) reduces the subsequent risk of AD in high-risk group with a positive family history. Co-existing allergic contact dermatitis is often overlooked in AD patients. Patch testing should be considered in AD patients who fail to respond to treatment, patients with atypical/changing distribution, hand eczema in working population, or before initiation of immunosuppressants.

Methyisothiazolinone present in wet baby wipes can cause perianal dermatitis. Other sources include fabric softener, hair shampoo/conditioner and paint.

Port-wine stains follow the lines of mosaicism. The somatic mutation involves the GNAQ gene. Frontotemporal, hemifacial and median patterns predict a higher risk of Sturge-Weber syndrome.

Learning points:

Coxsackie A6 infection may present with atypical HFMD. Early use of emollient and appropriate use of patch test improves outcome in AD patients.

Phototherapy for paediatric skin conditions

Speaker: Mark Koh

Department of Dermatology, KK Women's & Children's Hospital, Singapore

Phototherapy can be used for children with photo-responsive dermatoses that are not adequately controlled by topical medications alone. Phototherapy carries lower risks than systemic immunosuppressive agents. Some of these photo-responsive dermatoses include psoriasis, atopic dermatitis, vitiligo, mycosis fungoides and pityriasis lichenoides. Narrow band UVB is the most utilised form of phototherapy for children. Topical PUVA is an

alternative option in selected conditions. Targeted phototherapy can be used for localised lesions to avoid unnecessary UV exposure of unaffected skin. When phototherapy is indicated, it is crucial to consider the ethnicity and skin type of patient and the corresponding risk of carcinogenesis. Phototherapy should be performed by physicians and nurses who are experienced in managing children, in a child-friendly environment.

Learning points:

Phototherapy can be a useful treatment modality for photo-responsive dermatoses in children.

Update on the management of rosacea

Speaker: Alex WS Lam

Dermatologist, Private Practice, Hong Kong

Rosacea is a common chronic inflammatory facial skin condition. It can be classified into four subtypes according to clinical features which may overlap. These include erythematotelangiectatic rosacea, papulopustular rosacea, phymatous rosacea and ocular rosacea. The pathogenesis of rosacea remains unclear. The possible causative factors include exaggerated immune response, neurovascular dysregulation and impairment of skin barrier function. These factors serve as potential targets for intervention. As patients often have multiple concomitant facial inflammatory dermatoses, a multimodal tailored approach is often needed to tackle a wide range of symptoms.

Learning points:

An understanding of pathophysiology of rosacea can allow a more rational approach to rosacea treatment.

Pathogenesis of arsenical cancers in dermatology

Speaker: Abel CH Lee

Department of Dermatology, Kaohsiung Chang Gung Memorial Hospital, Taiwan

Arsenic is classified as a group I human carcinogen by the International Agency for Research on Cancer. Long term exposure to inorganic arsenic via ingestion or inhalation is associated with development of cancers in urinary bladder, skin, lung, kidney and liver in susceptible people. The most common arsenical cancer is skin cancer, among which Bowen's disease, a carcinoma in situ, comprises the majority. Microscopically there is epidermal keratinocyte proliferation, abnormal differentiation and moderate immune cell infiltrates. After decades, it may become invasive and penetrate basement membrane. Multidisciplinary approach has been utilised to investigate the molecular mechanisms of arsenic carcinogenesis, including mitochondrial regulations and immune interactions. Arsenic is found to increase mitochondrial oxidative stress which contributes to increased oxidative damage and mutations to mitochondrial DNA in keratinocytes and in tumour tissue of patients with arsenical skin cancers. Aberrant mitochondrial biogenesis mediates the arsenic-induced proliferation in keratinocytes. Chromosomal abnormality, oxidative stress and altered growth factors may be involved in arsenic carcinogenesis. Mitochondria, particularly its biogenesis, might be a potential therapeutic target for the arsenic-induced skin malignancies.

Learning points:

The interaction of abnormal immune responses and aberrant cell proliferation in arsenic-induced Bowen's disease provides a good model to study the early stages of chemical carcinogenesis.

Update on severe cutaneous adverse reactions (SCAR)

Speaker: Wen-hung Chung

Department of Dermatology & Drug Hypersensitivity Clinical and Research Center, Chang Gung Memorial Hospital, Taiwan

The clinical presentations of drug hypersensitivity may vary from mild maculopapular exanthema to severe, life threatening severe cutaneous adverse drug reactions (SCAR), including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS).

A number of important pharmacogenomic associations with SCAR have been found in different populations. Some specific HLA alleles are strongly associated with drug induced hypersensitivity reactions, such as HLA-B*15:02 for carbamazepine induced SJS/TEN, HLA-B*58:01 for allopurinol hypersensitivity, HLA-B*57:01 for abacavir hypersensitivity and HLA-B*13:01 for dapsone hypersensitivity. In contrast, many other

drugs induced hypersensitivity reactions did not show a highly HLA restricted manner. Preferential T cell receptor (TCR) clonotypes play a crucial role for SCARs. Activation of specific T cells expressing preferential TCR interacts with drug-specific HLA allele and culprit drugs in the immune mechanism.

Drug metabolism may also contribute to the pathogenesis of SCAR. In allopurinol-SCAR, studies have showed that coexistence of HLA-B*58:01 and renal impairment increased the risk and predictive accuracy of allopurinol hypersensitivity. The drug, ethnicity, phenotype specific association and paucity of cases increase complexity for pharmacological studies in SCAR.

Learning points:

Recent genome wide association studies or whole genome sequencing may help to find out more missing genetic links in SCAR.