

CUHK Dermatology Symposium 2006

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Date: 29 October, 2006
 Venue: Postgraduate Education Centre,
 Prince of Wales Hospital, Shatin
 Organiser: Dermatology Research Centre,
 The Chinese University of Hong Kong

Update on paediatric skin infections

Speaker: Dr. David Luk
 Department of Paediatrics, United Christian Hospital,
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Bacterial, viral and fungal infections are common in children but seldom life threatening.

Molluscum contagiosum has a tendency to infect atopic patients, may aggravate eczema, and may be complicated by secondary bacterial infection. Treatment is often preferred to prevent the child being left out from social activities and may include short contact potassium hydroxide or by cryotherapy. Special ways of handling children may be required for struggling children. Viral warts are also commonly seen in children and may be treated with cryotherapy. Careful history and communication with the family and patient is essential to identify potential sexual abuse but warts may also be caused by contact spread. Cryotherapy and podophyllin may be used for perianal warts.

Children with eczema have altered skin immunity which predisposes them to more severe viral infection. Eczema herpeticum is an important infection to recognise in atopic patients and may present as a flare up of eczema with oozing vesicles. It may be localised to the face and upper

chest or become generalised, and may become rapidly progressive with high mortality. Prompt treatment with intravenous acyclovir is essential. Consideration of stopping topical steroids and topical calcineurin inhibitors should be given. Scabies can also be associated with eczema and the pathognomonic scabetic nodules may often be seen over the genitalia in children.

Herpes simplex virus may present as herpes gingivostomatitis, herpetic whitlow, herpes simplex, and disseminated herpes. Herpes in the genital area should raise the suspicion of sexual abuse. Varicella may be very itchy in children with atopic eczema, while for herpes zoster, prodromal pain and post-herpetic neuralgia is uncommon in children. Ramsay-Hunt syndrome and ophthalmic herpes will require immediate therapy with acyclovir. Other common viral infections encountered in children were discussed. Roseola infantum may be associated with a high risk of febrile convulsion. Slapped cheek syndrome from parvovirus B can rarely result in aplastic anaemia. Coxsackie virus infection may have a risk of encephalitis. Measles may present as non-specific maculopapular eruption but examination of the oral cavity will show the pathognomonic Koplik's spots. Gianotti Costi syndrome is a self-limiting condition presenting with fever and papular lesions over the limbs.

Staphylococcal infections of the skin have always been the most common bacterial skin infection and have an important role in causing eczema flares. Occasionally *Staphylococcus aureus* may result in staphylococcal scalded skin syndrome and staphylococcal toxic shock syndrome. Therefore the importance of good wound management cannot be underestimated. Meningococcaemia

presenting as purpura fulminans must be treated promptly by antibiotics even before the child is transported to hospital due to rapid progression and associated high mortality.

Uncommonly, erythema nodosum may be encountered as tender nodules over the shins or erythema induratum as nodules that may ulcerate over the posterior calves. Underlying tuberculosis should be searched for and the BCG scar should be examined.

Common fungal infections encountered in children include dermatophyte infections of the trunk, feet and nails. Tinea pedis may present as a blistering eruption. Tinea capitis is less common nowadays as a result of improved hygiene and living conditions. Axillary scaling may be a result of erythrasma. Pityriasis versicolor is also common and may be treated with a course of oral itraconazole for 5 days.

Learning points:

Skin infections are common in the paediatric age group but rarely they can be life threatening. It is important to have a high index of suspicion in identifying infections which may have serious consequences and be aware of clues that may suggest sexual abuse.

Allergy genetics in Chinese children

Speaker: Professor Leung Ting-Fan
Associate Professor, Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong

Allergy is the commonest chronic disease worldwide and consists of a classical triad of asthma, allergic rhinitis and atopic dermatitis. Many susceptible patients with allergies undergo an 'atopy march' in which they first develop food allergy and atopic dermatitis during infancy, which are followed by the occurrence of asthma and allergic rhinitis 2-3 years later.

Atopy, commonly defined as the presence of allergen-specific IgE by skin prick testing or detection of such antibodies in peripheral blood, is closely linked to allergic diseases. These complex diseases are caused by an intricate interplay between genetic predisposition and environmental influences. The elucidation of candidate genes for allergy and atopy is crucial in understanding their pathogenesis and also in predicting the risk of an individual having these conditions later.

Traditionally, genetic predisposition to allergic diseases may be assessed by either genome-wide linkage analysis or the candidate gene approach. The target population can either be a cluster of families with affected children, in which the genetic association may be tested by transmission disequilibrium, or in unrelated case-control cohorts, in which we can evaluate the selective over- or under-representation of candidate gene alleles among patients and non-allergic controls. This latter approach has the merit of detecting a smaller genetic effect, but it usually requires a much larger sample size.

Over the past 7 years, our group has been studying intensively on allergy genetics in Chinese children using mainly the case-control genetic association approach. The genes which we genotyped include cytokines (IL13, IL1B, IL1RN, IL4RA, STAT6), chemokines and mediators of airway inflammation (FCER1B, TBXA2R, NOS1, NOS2, NOS3, CTLA4) and bronchial smooth muscle tone (ADRB2). A number of these candidate genes showed significant association with total and allergen-specific IgE in peripheral blood (IL13, TARC, CD14, DEFB1, NOS1, CTLA4, TBXA2R and ADRB2) and, to a lesser extent, asthma (DEFB1, TARC, TBXA2R and MBL2), lung function (RANTES, TBXA2R, STAT6 and IL1B) and peripheral eosinophilia (TARC and DEFB1) in local children. Some of these associations were not found in other ethnic groups. Our group also found significant interethnic variations in the minor allele frequencies of many of these candidate genes for allergy and atopy in Chinese children as compared to Caucasians and other Asians. Recently, our group published significant gene-gene interactions for conferring risks to asthma

(IL13 and IL4RA) and increased plasma total IgE concentration (IL13 and TARC) when a panel of 12 single nucleotide polymorphisms from eight candidate genes were analyzed by multifactor dimensionality reduction. In conclusion, the genetics of allergic diseases in Chinese children is complex and cannot be extrapolated directly from the results published in other populations.

Learning points:

Atopy and the closely linked allergic diseases involve an intricate interplay between genetic predisposition and environmental influences. Local studies of allergy genetics in Chinese children using the case-control genetic association approach have been useful in genotyping relevant cytokines, chemokines and various mediators, identifying interethnic variations of candidate genes and significant gene-gene interactions conferring risks to asthma and IgE.

Advances of laser in treating skin diseases

Speaker: Dr. William KK Fung

Specialist in Dermatology, Private Practice, Hong Kong

Laser systems have been developed for treatment of skin diseases and beautification for over a decade. In recent years, new concepts of laser technology continue to evolve, driving the manufacture of new laser systems at a very speedy pace.

The refinement of existing laser systems in terms of energy output, wave form, pulse width adjustment, operation speed, etc. has rendered the operation safer, faster and more cost effective while producing better clinical efficacy and outcome. Examples of these include larger spot size and faster operation speeds of new systems for hair removal, new non-laser intense pulsed light (IPL) systems emitting square wave

pulses with very large spot size and multiple cut off filters for various pigmented and vascular lesions, as well as photorejuvenation.

New concepts in the treatment of specific diseases have appeared in recent years. Daily Q-switched laser therapy for melasma and cafe-au-lait macules (CALM) is based on additive sublethal damage to melanocytes. The plasma kinetic skin resurfacing concept provides the basis of fractional resurfacing for wrinkle reduction. The aim of newer systems is to improve clinical efficacy and safety for targeted skin problems, with reduced downtime and cost.

Other newly developed laser systems include ablative fractional resurfacing lasers for skin tightening, fractional infrared lasers for rejuvenation and combination systems (e.g. radiofrequency device plus infrared laser). Lasers for cellulite therapy are still in the experimental stage.

Combination therapy using different laser systems, or lasers with other non-laser modalities (e.g. IPL systems, microdermabrasion, botulinum toxin injection, fillers, light emitting diode (LED) devices etc.) has been found to achieve better clinical results for certain skin problems, such as acne scars and wrinkles, compared with cases using single laser systems.

The future trend in laser advancement is the appearance of small sized home devices for skin rejuvenation, acne therapy and hair removal. Low energy LED devices for photorejuvenation have been developed for sale in the market for home use.

Learning points:

Continuing evolution and refinement of laser technologies and new concepts in the treatment of skin diseases have provided much improved safety and clinical efficacy in treating various skin problems.

Update on the management of cutaneous manifestations of rheumatological diseases

Speaker: Dr. Tam Lai-Shan

Associate Professor, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong

Cutaneous lupus erythematosus (CLE) can be divided into lupus specific and lupus non-specific type, as defined by the presence of 'characteristic' histology of LE. Lesions that are histologically specific for lupus erythematosus are divided into acute, subacute and chronic CLE.

Malar rash is a photosensitive erythematous confluent rash involving both malar eminences and crosses the nose bridge, being often referred to as butterfly rash. It is a form of acute CLE. It is associated with active systemic disease and will subside without any scars once the disease is under control with steroid or immunosuppressant.

Subacute cutaneous lupus erythematosus (SCLE) accounts for 10-50% of CLE. It is a non-scarring, non-atrophy-producing photosensitive dermatosis and may occur in SLE, Sjogren syndrome, C2 deficiency and drug-induced case. It is more common in whites. Fifty percent fulfill the diagnosis of SLE and serologic abnormalities are common. The male-to-female ratio in SCLE is 1:4. The morphology can be papulosquamous or annular.

Discoid lupus erythematosus (DLE) is a chronic, scarring, atrophic, photosensitive dermatosis. DLE may occur in patients with systemic lupus erythematosus (SLE), and less than 5% will progress to systemic disease. DLE is responsible for 50-85% of CLE. DLE is slightly more common in African Americans than in whites or Asians. The male-to-female ratio in DLE is 1:2. DLE may occur at any age but most often in persons aged 20 to 40 years. The mean age is approximately 38 years.

Lupus profundus involves subcutaneous lobular lymphocytic inflammation with or without overlying surface change of DLE. Subcutaneous calcification may occur and can produce considerable disability

from secondary cutaneous ulceration and infection. However, there is relatively little risk of association with SLE.

Lupus tumidus refers to photosensitive urticarial plaques over the face, neck, upper trunk, and proximal upper extremities. It involves deeper level and is more nodular with little scaling. Chilblain LE is cold-induced violaceous plaque affecting acral aspect of extremities and persists beyond the cold season.

The treatment options are divided into local and systemic measures. Sunscreen is advisable to block both the UVA & UVB. Local therapies include topical or intralesional steroid, and topical tacrolimus. Single-agent or combined aminoquinoline anti-malarial therapy e.g. hydroxychloroquine, hydroxychloroquine and quinacrine or chloroquine and quinacrine, is the initial systemic treatment of choice. Other options include thalidomide, retinoids, dapsone, gold, clofazimine, prednisone, methotrexate, azathioprine, cyclosporin, and mycophenolate. Among these, thalidomide is the most efficacious drug for anti-malarial-refractory cutaneous LE, but its clinical utility is limited by its adverse effects.

The cutaneous manifestations of dermatomyositis (DM) include gottron's papule, heliotrope rash, mechanics hands, shawl sign and V-sign. For the relationship between cutaneous and systemic manifestations of DM, 60% skin and muscle changes appear together, 30% skin lesion precede muscle weakness by weeks or months, and 10-20% skin lesion occurs as isolated clinical findings for more than 6 months beforehand, being called amyopathic dermatomyositis (ADM). ADM is defined by typical cutaneous disease and no evidence of muscle weakness, with normal serum muscle enzyme levels repeated for more than 6 months in the absence of disease-modifying therapies and abnormal findings on sonogram, MRI, or muscle biopsy.

For treatment, UVB & UVA blocking sunscreen is advisable. Local therapies include emollients, topical or intralesional steroids and topical tacrolimus. Systemic therapies include

hydroxychloroquine, combination of hydroxychloroquine and quinacrine or chloroquine and quinacrine. If these fail, other options include dapsone, prednisone, methotrexate, azathioprine, cyclosporine, mycophenolate, and intravenous immunoglobulins. It was found that elevated level of TNF- α and its soluble receptors in muscle biopsy might be directly toxic to myofibers, while preventing muscle regeneration. TNF inhibitor and B cell depletion therapy might have its role in future.

Learning points:

The multi-facet nature of rheumatological cutaneous lesions calls for vigilance and completeness in clinical examination as well as laboratory verification.

Update on bacterial skin infections

Speaker: Professor Margaret Yip
 Department of Microbiology, The Chinese University of Hong Kong, Hong Kong

Staphylococcus aureus is a major cause of skin and soft tissue infections including impetigo, folliculitis, cellulitis, erysipelas, scalded skin syndrome and toxic shock syndrome. According to Reuters Health Information reported in 2006, methicillin resistant strain of *Staphylococcus aureus* (MRSA) is the most common cause of skin and soft-tissue infections in major US cities. It can be community acquired (CA) and hospital acquired (HA). Community-acquired MRSA (CA-MRSA) is defined as MRSA infection diagnosed in an outpatient setting or by a positive culture of MRSA within 48 hrs of hospital admission with the exclusion of any medical history of MRSA infection or colonisation, past medical history including hospitalisation, admission to a nursing home or institution, dialysis, surgery, and no permanent indwelling catheters or medical devices. MRSA often affects healthy people and presents as skin infections such as boil or abscess by skin contact. It can also occur in clusters such as athletes, military personnel, children, prisoners etc. Its characteristic is resistance to oxacillin but sensitivity

to multiple drugs. Staphylococcal chromosomal cassette *mec* (SCC*mec*) type IV, clonal type ST30, panton-valentine leukocidin (PVL) gene are also present. The major differences between HA- and CA- MRSA are summarised in the following table:

HA-MRSA	CA-MRSA
Healthcare contact	No healthcare contact
>50 years old	<20 years old
Bacteraemia	Skin and soft tissue infections, necrotizing pneumonia
Resistant to β -lactams	Resistant to β -lactams
Multidrug resistance (MDR) to clindamycin, gentamicin, fluoroquinolones	Usually only resistant to erythromycin, fluoroquinolones
SCC <i>mec</i> I, II or III	SCC <i>mec</i> IV or V
PVL rare (5%)	PVL positive (95%)
Clones ST239, 5 etc.	Clonal type ST30

The risk factors for CA-MRSA infections include history of previous MRSA infection or colonisation in patient or close contact, high prevalence in local community, recurrent skin diseases, crowded living condition, frequent or recent antibiotic usage, and children under 2 years of age. In Hong Kong, there were 25 episodes (23 cases) of CA-MRSA from January 2004 to December 2005. Twenty-four episodes were skin and soft tissue infections and 1 episode was meningitis. For those presenting with skin and soft tissue infection, majority presented as furuncles or carbuncles. Other presentations included perianal abscess, deep seated thigh infection, infected sebaceous cyst and scalp abscess. The mean age was 28 years ranging from 13 months to 91 years. Three children had eczema, 1 patient was a hepatitis B carrier and the rest had no underlying disease. Most cases resolved with incision and drainage, with or without antibiotics.

Concerning the management of CA-MRSA, the primary therapy is adequate incision & drainage of abscess, and to obtain material for culture if

possible. The suitable choice of antibiotics can be either topical or systemic but the latter is preferred. For the systemic route, cotrimoxazole, clindamycin, and minocycline are treatment options while macrolides and fluoroquinolones are not recommended because of the increased risk of resistance. Topical 2% mupirocin can also be used. The patients should be advised to come back if there is no improvement within 48-72 hours. It can also occur as carrier status. The sites with highest sensitivity for MRSA screening are nose, throat and perineum (up to 98.3%). There are various methods used to eradicate MRSA carriage: 2% mupirocin applied over nasal mucosa 3 times per day for 5 days, rifampicin with fusidic acid or ciprofloxacin for 5 days applied in throat in refractory cases or outbreak situation, 4% chlorhexidine bath for 5 days or shampooing hair 2 times weekly with antiseptic detergent. Finally, contact precautions are also important such as handwashing, personal protective equipment, and environmental cleansing.

Learning points:

Sound microbiological knowledge and cautious infection control measures are the best armaments against the common but sometimes very noxious *Staphylococcus aureus* skin infection.

Pregnancy related dermatoses

Speaker: Dr. Shirley W Chan

Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong

Pregnancy related dermatoses included 1) polymorphic eruption of pregnancy, 2) pemphigoid gestationis, 3) prurigo of pregnancy, 4) pruritic folliculitis of pregnancy, 5) impetigo gestationis, 6) cholestasis of pregnancy, 7) eczema of pregnancy.

The term atopic eruption of pregnancy was proposed by Ambros-Rudolph and MM Black to include eczema of pregnancy, prurigo of

pregnancy, pruritic folliculitis of pregnancy and papular dermatitis of pregnancy.

In polymorphic eruption of pregnancy (PEP) (Pruritic urticarial papules and plaques of pregnancy, PUPPP), pruritic erythematous eruption occurs in the second half of pregnancy or immediate post partum. It may be related to damage to connective tissue or elastic fibres within striae distensae, hormonal factors or fetal factor. The condition is self limiting and tends not to recur in subsequent pregnancy. It does not affect the fetal outcome and is not associated with changes in fetal and birth weight. Management is symptomatic with emollients, topical corticosteroids and chlorpheniramine. Systemic steroid is rarely needed.

Pemphigoid gestationis is associated with hydatidiform moles, choriocarcinomas, Graves' disease, HLA-DR3 (61-80%), HLA-DR4 (52%) or both (43-50%). The target antigen is BP 180 (BP antigen 2, type XVII collagen) transmembrane protein in hemidesmosome. The main epitopes are restricted to the noncollagenous domain NC-16A found in placenta after second trimester. The onset is in 2nd or 3rd trimester, rarely in postpartum. Spontaneous remission occurs in weeks or months after delivery. The condition tends to recur in subsequent pregnancy. Flare with oral contraceptive pills was reported. The condition starts in the umbilical region in 50% of the cases while sparing the mucosa. It presents with pruritus and urticated lesions initially. Progress to blisters is noted in days or weeks. Systemic corticosteroid is used to treat this condition. There is an increased risk of small for gestational age and premature delivery. However, there is no increase in fetal mortality. Transient blisters or urticated lesions are noted in up to 10% of the babies due to transplacental transmission of maternal antibodies. Indirect IMF with enzyme linked immunosorbent assay (ELISA) detecting BP 180 IgG antibodies to the extracellular domain (NC-16A) is a potential useful tool in the future.

Prurigo of pregnancy occurs more in patients with an atopic tendency. The onset is 25 to 30 weeks. It does not recur in subsequent pregnancy.

Excoriated papules and nodules are found and there is no specific laboratory or histopathological finding in this condition.

In pruritic folliculitis of pregnancy, follicular papules with sterile pustules are found clinically and perifolliculitis is noted in the histopathology. It occurs at 4 to 9 months gestation. It does not recur in next pregnancy and there is no adverse fetal outcome. Treatment needs only mild topical steroid and benzoyl peroxide.

Impetigo herpetiformis (IH) is a rare specific dermatosis of pregnancy. The onset is in 3rd trimester. It resolves soon after delivery and tends to recur in subsequent pregnancy or even with menstruation or oral contraceptive pills. The condition may start in flexural regions and spread centrifugally, forming polycyclic plaques with pustules over the periphery. It does not have flare after withdrawal of systemic steroid. The histology is similar to generalised pustular psoriasis (GPP). Most authorities believe that it is a specific condition, though IH may develop in patients with a history of plaque psoriasis. The condition is associated with electrolyte problems, hypocalcaemia, hypoparathyroidism and sepsis. Placental insufficiency may also be found and is associated with fetal abnormality, stillbirth and neonatal death. The management of this condition is supportive. Systemic corticosteroid and cyclosporin may be needed.

In cholestasis of pregnancy (intrahepatic cholestasis of pregnancy = obstetric cholestasis = prurigo gravidarum), secondary changes due to itch, e.g. excoriations are found. The incidence is 0.02-2.4% and it occurs more in twin pregnancy. Seventy percent recurs in next pregnancy. Increased total bile acids, alkaline phosphatase, bilirubin, cholesterol, lipids are found. It is associated with increased incidence of stillbirth and premature birth, postpartum haemorrhage and fetal intracranial haemorrhage due to vitamin K malabsorption. Treatment options include cholestyramine, ursodeoxycholic acid, phenobarbitone and phototherapy to reduce itch. Anti-histamine is not effective.

Eczema in pregnancy is probably the commonest pruritic condition in pregnancy. Pruritic eruption is found more over the flexural areas. It has a variable or early onset. The patients may have a past or family history of atopy or raised IgE.

Learning points:

Advances in molecular biology have contributed to a better understanding of the specific dermatoses of pregnancy and hence a better therapeutic approach and prognostic predictability. However, the aetiopathogenesis remains unclear in most entities. It is important to recognise the diagnosis and initiate appropriate treatment. Potential fetal and maternal risks must be identified. A team approach that involves dermatologist, paediatrician, and obstetrician is helpful.

Recent advances in topical treatment of melasma

Speaker: Dr. Cheong Wai Kwong
Specialist Skin Clinic, Singapore

Melasma may affect up to 4% of some populations in Southeast Asia. It is more commonly seen in patients of skin type III to VI. It is related to solar radiation and hormonal changes. About 90% of cases are women.

Centrofacial melasma is the most common (64-70%) type of melasma, affecting forehead, nose, chin, central (flush) area of cheeks and upper lip region. It is important to differentiate between the epidermal and the dermal varieties as the epidermal variety responds better to treatment. Pigmentation is intensified in the former but less prominent in the latter variety under Wood's light examination.

Treatment strategies of melasma include protection from the sun, inhibition of tyrosinase activity, removal of melanin and blocking transfer of melanosomes. Hydroquinone, tretinoin, topical

steroids and azelaic acid are established topical treatments for melasma. However, hydroquinone or tretinoin monotherapy may lead to possible post-inflammatory hyperpigmentation resulting from irritant dermatitis which is more common in dark skinned persons. Moreover, prolonged duration of treatment may be required for meaningful results.

Hydroquinone has been used in combination with other agents to improve efficacy and minimise adverse effects. The original combination treatment was developed by Kligman and Willis in 1975. Dermatologists worldwide have used compounded formulations. However, these formulations are unstable, not standardised and prone to oxidation. The proposed mechanism of action include 1) tretinoin reduces atrophogenic effect of steroid 2) tretinoin facilitates the epidermal penetration of hydroquinone 3) the steroid helps reduce irritation caused by tretinoin. The results were significantly less favourable if one of the components were omitted.

Tri-Luma® cream (hydroquinone 4%, tretinoin 0.05%, fluocinolone acetonide 0.01%) is a stable formulation of a recognised compounded formula. It has a longer shelf life than compounded formulations and is cosmetically elegant. It is found to be an effective and safe

treatment for melasma. Seventy-three percent cleared or nearly cleared at 1 month and the figure rose to 81% at 12 months. There was no increase in severity of adverse events observed in long term use over 8 week controlled study. An excellent safety profile was noted even after 12 months.

To effectively manage melasma, the following points should be noted: (1) make the right diagnosis e.g. Hori's naevus might cause confusion, (2) assess the skin type and beware of sensitive skin type or aged skin, (3) good sun protection: daily use of broad spectrum sunscreen with SPF greater or equal to 30, (4) note details of previous treatments, (5) optimise the use of Tri-Luma by discontinuing all existing skin care product if unsure of interaction and treating any existing dermatitis before starting using Tri-Luma, (6) go slow when treating sensitive skin, and (7) avoid topicals that dry the skin.

Learning points:

A combination of hydroquinone, tretinoin and steroid is useful in the treatment of melasma. Tri-Luma®, a stable formulation of a recognised compounded formula, is found to be effective and safe in treating melasma.