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Reports on Scientific Meetings

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The war on molluscum: report from the front lines

Speaker: Seth Orlow
Ronald O. Perelman Department of Dermatology, NYU Langone Medical Center, USA

Molluscum contagiosum is a viral disease caused by a DNA poxvirus. The incubation period is usually two to seven weeks. Molluscum contagiosum virus I is the most prevalent. Molluscum contagiosum tends to be more common in children with a history of atopy. Lesions typically occur on the chest, arms, trunk, legs and face. The palms are spared. Molluscum contagiosum in healthy children and adults is usually a self-limiting disease.

Cantharidin was originally derived from the blister beetle and is an inhibitor of protein phosphatase 2A. It causes dissolution of desmosomal plaque, leaving dermis intact and is one of the treatment options for molluscum contagiosum.

Inflamed molluscum contagiosum lesions and Gianotti-Crosti syndrome–like reactions reflect cell-mediated immune responses that herald viral clearance. Treatment of molluscum dermatitis with appropriate topical corticosteroids reduces the itching and autoinoculation. The prognosis in molluscum contagiosum is generally excellent because the disease is usually benign and self-limited. Molluscum contagiosum will likely last 12 to 24 months.

Learning points:

Molluscum contagiosum is a viral disease caused by a DNA poxvirus. The prognosis is generally excellent because the disease is usually benign and self-limited.

Hair disorders in children

Speaker: Manabu Ohyama
Department of Dermatology, Kyorin University School of Medicine, Japan

Management of hair loss disorder in children is sometimes challenging, partly because of the difficulties in medical history and limited treatment options. Approaches to hair loss disorder include pattern analysis, morphological examination and physical examination for other

signs, e.g. nail change. Alopecia areata is a non-scarring autoimmune disease of the hair follicle that can present at any age. Alopecia areata is the most common form of child hair loss encountered in daily practice. Dermoscopy is a pivotal tool in the diagnosis of hair loss diseases. The most common dermoscopic findings in alopecia areata include yellow dots, black dots, broken hairs, short vellus hairs and tapering hairs. Alopecia areata and trichotillomania more frequently co-exist in paediatric cases. However, detection of accompanying trichotillomania may be difficult in some cases. Dermoscopic signs, represented by follicular micro-haemorrhage, are useful in the diagnosis of two co-existing conditions.

Genetic approaches provide powerful tools for the diagnosis of congenital hair diseases. For those with total hair loss, histopathological investigation is also valuable in differentiating congenital alopecia areata from other conditions. Assessment of symptoms other than alopecia should better include direct gene mutation analysis, particularly in the cases with total hair loss.

The Japanese Dermatological Association guidelines recommend contact immunotherapy for severely affected paediatric cases of alopecia areata. For those with longstanding alopecia totalis/universalis, reversal of the condition would be challenging. JAK inhibitors or regenerative medicine hold promise as future therapeutic options.

Learning points:

Approaches to hair loss disorder include pattern analysis, morphological examination and physical examination for other signs. Dermoscopy is a pivotal tool in the diagnosis of hair loss diseases.

New approach in the management of facial redness in rosacea

Speaker: Gregor Schaefer
Dermatologist, Global Medical Expert, Galderma, Germany

Rosacea is a chronic inflammatory condition whose pathophysiology encompasses neural, vascular and inflammatory components. It affects emotional and social well-beings in those affected. Persistent (non-transient) erythema is a stigmatising symptom of rosacea caused by increased skin blood flow. Brimonidine gel (Mirvaso) is a selective alpha-2 adrenergic receptor agonist which constricts skin blood vessels and reduces erythema. In clinical studies, it has been shown to reduce erythema compared to vehicle when applied once daily. Its effect appears as soon as 30 minutes after application. Long-term efficacy in terms of continued improvement at 3 hours over a 12-month period has been observed and tachyphylaxis is not reported. Adverse effects are usually mild and transient, and include flushing, erythema, burning sensation, irritation and pruritus. Up to 9.7% of patients reported moderate to severe adverse effects. Caution (from package insert) is advised in patients with depression, cerebral, coronary or vascular insufficiency, and when used with drugs such as beta-blockers, anti-hypertensives, cardiac glycosides and monoamine oxidase inhibitors. Erythema can be classified as early onset (3-6 hours); expected onset (8-10 hours); late onset (more than 12 hours) and very late onset (in terms of months). It has been suggested that the identification and control of triggers and treatment of inflammatory lesions should make up integral elements in the treatment approach.

Learning points:

Brimonidine gel is an efficacious daily topical application for erythema in rosacea but its adverse effect of erythema should not be overlooked.

Management of hair loss disorders in Japan – Introduction of our guideline and new insights

Speaker: Manabu Ohyama
Department of Dermatology, Kyorin University School of Medicine, Japan

The pathophysiology of alopecia areata (AA) differs greatly between acute and chronic phase. In acute phase, inflammatory cell infiltration around the perifollicular area of anagen hair follicles is remarkable, while in chronic phase most hair follicles are in telogen phase with minimal cell infiltration.

Japanese Dermatological Association (JDA)'s guidelines suggest the use of anti-inflammatory treatments for acute AA and immunomodulatory therapy such as contact immunotherapy for chronic AA. A study of 139 patients showed intravenous pulse corticosteroid therapy could provide effective remedy for acute and severe cases of AA. In JDA's guidelines, criteria for this therapy include age above 15, more than 25% but not 100% of the scalp surface area affected, rapidly progressive and within 6 months from the onset of hair loss.

Cumulative evidence together with the high incidence of AA in those with atopic background suggests that antihistamines such as fexofenadine, olopatadine and ebastine are effective in AA. A study using a mouse model of AA also supports this concept.

For male androgenic alopecia (AGA), minoxidil and finasteride are still the standard treatments. Dutasteride, a dual 5α–reductase inhibitor, showed promising results for the treatment of AGA from clinical studies. Only minoxidil has been recommended for female AGA in JDA's guidelines, illustrating the current limitations in treating this condition.

Learning points:

The launch of the JDA guidelines enables better management of hair loss diseases, represented by AA and AGA.

Management of non-infectious nail disorders

Speaker: William Tang
Dermatologist, Private Practice, Hong Kong

Dr. Tang performed a survey of case records on nail diseases in new patients who attended his clinic over a five-year period. A total of 139 cases and 195 cases were retrieved and classified into infectious and non-infectious nature respectively. The commonest non-infectious nail disorder was onycholysis (26% of all non-infectious cases). General treatments include minimising trauma to the affected nail, reducing contact to water, avoiding irritant environments, using protective gloves for wet work, stopping nail cosmetic and clipping the onycholytic portion short in regular intervals. Topical antiseptic such as 2-4% thymol in chloroform and topical antifungal can be used to reduce the risk of secondary infection. Topical steroid lotion may be tried for persistent singly affected nail without evidence of infection.

Treatments of some other common non-infectious nail disorders were also discussed. The first-line treatment for nail psoriasis is high-potency topical corticosteroids +/- calcipotriol. The management of chronic paronychia including general nail protective measures as mentioned for onycholysis; topical steroid, antifungal or tacrolimus may be helpful. The majority of cases of paediatric trachyonychia improve with time, regardless of treatment. Dermoscopy is a helpful tool for evaluating melanonychia. As longitudinal melanonychia in childhood is typically associated with benign stable melanocytic proliferations, biopsy is seldom required. Conservative treatments for ingrown nails include gauze pledget and gutter splint. As surgical wedge excision can be very bloody, phenol matricetomy may more suitable for the dermatology clinic.

Learning points:

Non-infectious nail disorders are common and it is important to know their management.

Rheumatological manifestations of dermatological disorders

Speaker: Chak-sing Lau
Department of Medicine, Queen Mary Hospital, Hong Kong

There is a close relationship between rheumatology and dermatology disciplines. Many rheumatological and dermatological conditions are manifestations of systemic disorders with immune-mediated pathogenesis, such as systemic lupus erythematosus, systemic sclerosis, dermatomyositis and necrotising vasculitis. Sometimes joint diseases such as erosive peripheral arthritis and/or spondylitis may develop in a proportion of patients with underlying dermatological diagnosis of cutaneous psoriasis. A number of dermatological conditions may initially present with joint or back pain, Raynaud's phenomenon and autoimmune serological changes. On the other hand, patients with rheumatoid arthritis, spondyloarthritis and gout may first present with mucocutaneous signs.

Professor Lau used three clinical scenarios to illustrate the relationship of rheumatological and dermatological diseases. Case 1 was a patient with Sweet syndrome. The patient presented with recurrent fever, polyarthralgia and tender pustular nodules. Blood results showed an increase in inflammatory markers, liver enzymes and skin biopsy showed diffuse neutrophil infiltration without leucocytosis or vasculitis. Case 2 was a patient with SAPHO syndrome (Synovitis, Acne, Pustulosis, Hyperostosis, Osteitis): The patient presented with fever, back pain, increase in inflammatory markers and abnormal MRI findings. After treatment by systemic antibiotics for five months, the clinical condition went into remission but relapsed after one year. On further examination, acneiform lesions over the trunk and pustulosis over the palms were found which suggested the diagnosis. Case 3 was a patient with psoriatic arthropathy presenting with spondyloarthropathy and psoriasform plaques over the hairline and elbows.

Professor Lau also shared with the audience the diagnosis of psoriatic arthropathy, when to refer a patient with back pain to a rheumatologist, and the Systemic Lupus International Collaborating Clinic (SLICC) classification criteria for systemic lupus erythematosus.

Learning points:

Many rheumatological and dermatological conditions are manifestations of systemic disorders and they often share common pathogenic mechanisms. Liaison between rheumatologists and dermatologists is important in the diagnosis and patient care.

Novel therapy for seborrhoeic dermatitis: treatment and maintenance

Speaker: Wai-kwong Cheong
Dermatologist, Specialist Skin Clinic & Associates, Singapore

Seborrhoeic dermatitis has a worldwide prevalence of 1-5%. It is also common in Asia. It can affect both adults and children. The pathogenesis involves *Malassezia* yeast infection, sebaceous gland secretions, genetic susceptibility, immune dysfunction, and emotional stress. The pathogenicity and local distribution of the *Malassezia* species is affected by the ethnicity and climatic conditions.

Seborrhoeic dermatitis presents as a greasy scalp with dandruff and patchy erythema with scaling on the scalp, forehead, eyebrows, nasolabial folds and body folds, including the axillae and groin areas. Differential diagnoses included dermatophytosis, atopic eczema, psoriasis, rosacea and lupus erythematosus.

The current treatment options for seborrhoeic dermatitis are topical antifungal agents, topical steroids, and topical calcineurin inhibitors. A short

course of oral antifungal agent may be used for severe cases.

The speaker introduced Sebclair® cream as a new non-steroidal anti-inflammatory agent with antifungal properties. It may be applied three times per day. Investigator Global Assessment scores with respect to erythema and scaling showed a higher percentage of success in the Sebclair® group than the placebo group (68% vs 11%, $p<0.0001$). The speaker concluded that Sebclair® cream may be used as monotherapy or as well as maintenance treatment for seborrheic dermatitis of the face.

Learning points:

Seborrhoeic dermatitis is a chronic relapsing disorder. Long term maintenance treatment is needed. Sebclair® may be used for mild to moderate seborrhoeic dermatitis.

The Yin and Yang of microbes and atopic dermatitis

Speaker: Seth Orlow
Ronald O. Perelman Department of Dermatology, NYU Langone Medical Centre, USA

Microbes are commonly associated with atopic dermatitis and it is unclear whether they are opportunistic or contributory to the course of disease. Barrier dysfunction and immune dysregulation in atopic dermatitis result in colonisation and infection by specific microbes. *Staphylococcus aureus* is highly prevalent in atopic dermatitis and produces exotoxins that may act as superantigens to promote inflammation. Besides, up to two thirds of cases of atopy were shown to have evidence of IgE to *Malassezia* species by skin prick test or atopy patch test. However, the effects of azole antifungals in atopic dermatitis are conflicting.

Despite evidence that antimicrobial therapy is of marginal utility, it is commonly overutilised, engendering resistance without significant benefit. As a result, antimicrobial therapy should be administered only if there is overt evidence of infection.

Bleach baths have been shown to reduce the severity of disease in children with moderate to severe atopic dermatitis. Furthermore, probiotics have been demonstrated to prevent atopic dermatitis in infants when taken by pregnant women. However, most studies failed to demonstrate any benefit of probiotics in those already diagnosed with atopic dermatitis.

Learning points:

Overuse of antimicrobial treatment may result in resistance. Treatment of underlying atopic dermatitis should generally be the focus unless there is evidence of infection.

Update of allergy testing in paediatrics: component resolved diagnostics for food allergy

Speaker: Marco Ho
Department of Paediatrics and Adolescent, Queen Mary Hospital, Hong Kong

Food allergies significantly impair quality of life and may result in life-threatening reactions. Diagnosis of food allergy is needed to prevent significant reactions and to avoid unnecessary dietary elimination. However, clinicians are often challenged by inconsistent history and false positivity of skin prick tests and food specific IgE testing. Formal food challenge is a tedious procedure and carries potential risk.

The development of component-resolved diagnostics (CRD) is a breakthrough in food allergy testing. CRD detects specific IgE to individual allergens in diagnostic extracts and allows diagnostic improvement. More than 130 allergenic molecules are commercially available

for in vitro specific IgE testing. Studies have demonstrated that CRD might improve specificity of allergy testing to a variety of foods including peanut, milk and egg. CRD can be used to assess the risk for systemic reactions, to differentiate between genuine peanut allergy and pollen-related peanut allergy, and to ensure relevant dietary advice and avoid unnecessary elimination. The pitfalls of CRD are sensitivity issue, geographical variations and cost-utility issue.

Learning points:

Although molecular allergology diagnostic is a complex area, it provides novel and relevant information for the allergist and will soon become a standard tool in the allergist's armamentarium.

Pemphigus vulgaris: a retrospective review of the clinical features, treatment and prognostic factors over a 13 year period

Speaker: Ka-yee Kung
Department of Medicine, Queen Mary Hospital, Hong Kong

Pemphigus vulgaris accounts for 70% of pemphigus diseases. It is a severe disease with high mortality and morbidity. Mortality rate was 50% over two years and 100% over five years before the introduction of systemic steroids. Current mortality is estimated at 5%-10%. Recurrence rates are high and up to 98% even if initial remission achieved. A study recruiting 108 patients with pemphigus vulgaris was performed. The age of onset was between 47-54 years. Associated medical conditions for pemphigus were as follows: malignancy (6.48%), autoimmune disease (4.63%), hepatitis B (7.4%), cardiovascular disease/metabolic disease such as diabetes mellitus (DM), hypertension, ischaemic heart disease, stroke and peripheral vascular disease (3.42%). Mucocutaneous involvement was present in 73.1% of the patients and indicated more active disease and a worse prognosis. The site of involvement of pemphigus vulgaris was more often on the trunk rather than the mucosal area. Both systemic steroids and immunosuppressants were used for the treatment. The mean dose of systemic steroid was 33.93 mg and the total steroid dose was 1992.5 mg. The use of systemic steroid led to a worsening of DM control and azathioprine was occasionally complicated by liver impairment. The mean time to achieve control of pemphigus vulgaris was 9.1 weeks and earlier control of disease indicated earlier remission. The relapse rate was 51.2%. If both systemic steroids and immunosuppressants were required, the time to remission was usually longer.

Learning points:

Mucosal involvement of pemphigus vulgaris is indicative of more active disease and warrants more aggressive treatment with systemic steroid and immunosuppressant.

A study of point-of-care test to diagnose syphilis in Hong Kong

Speaker: Chiu-choi Koh
Social Hygiene Service, Department of Health, Hong Kong

In Hong Kong, most patients with syphilis are managed in the public sector under Social Hygiene Clinic (SHC). 'Point-of-care' test (POC) syphilis test is available and used by the some outreach medical teams of non-government organisations (NGO) to screen for syphilis among high-risk groups who are reluctant to have standard screening tests in the clinic. POC syphilis test also has the advantage of being able to give an immediate result, making "same day testing and referral" possible. This study aimed to determine the significance of POC syphilis test in screening syphilis among high-

risk groups in Hong Kong and to compare the diagnostic performance between two different brands of POC syphilis test commonly used in HK. Patients with aged above 18 years were recruited from two social hygiene clinics for the POC syphilis tests. New patients attending the social hygiene clinics, patients with newly diagnosed syphilis and patients with a history of treated syphilis were recruited from October 2012 to February 2013. Two different POC syphilis tests (Alere Determine™ Syphilis TP and SD BIOLINE Syphilis 3.0) were performed. Results were compared with conventional syphilis diagnostic tests: demonstration of typical spirochaetes in skin lesion by dark ground microscopy, *Treponema pallidum* enzyme immunoassay (EIA), *Treponema pallidum* particle agglutination assay (TPPA), *Treponema pallidum* haemagglutination antibody absorption test (FTA-Abs).

A total of 356 patients were recruited in the study to perform POC syphilis test. Ninety-one percent of patients were male and 9% were female. The stage of syphilis of of these patients was as follows: late latent syphilis (LLS) (67.3%), early latent syphilis (ELS) (8%), secondary syphilis (SS) (11.7%) and primary syphilis (PS) (12.3%). The overall result for Alere Determine™ Syphilis TP ("Alere Ltd", USA) was as follows: sensitivity 56.1%, specificity 100%. The overall result for SD BIOLINE Syphilis 3.0 (Standard Diagnostics, Inc., Korea) was as follows: sensitivity 57.4%, specificity 100%.

Learning points:

The POC syphilis tests evaluated in this local study were found to have a high specificity but a low sensitivity. They are not suitable for the use as a standard screening test for syphilis.

Immune mechanism and danger signals in severe cutaneous adverse drug reactions

Speaker: Wen-hung Chung
Department of Dermatology, Drug Hypersensitivity Clinical and Research Center, Chang Gung Memorial Hospital, Taiwan

The clinical manifestations of drug eruption range from mild maculopapular eruption (MPE) to severe, life-threatening drug-induced hypersensitivity syndrome, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). The common culprit drugs related to severe cutaneous adverse drug reactions are allopurinol, carbamazepine, phenytoin and lamotrigine. The findings of drug-specific genetic markers related to hypersensitivity reactions (e.g. *HLA-B*1502* for carbamazepine-induced SJS/TEN and *HLA-B*5801* for allopurinol-induced SJS/TEN/drug reaction with eosinophilia and systemic symptoms) provide a foundation for the personalised medicine by performing genetic tests before prescribing. The speaker conducted a genome-wide association study followed by direct-sequencing of the associated genes related to phenytoin hypersensitivity. The study revealed that *CYP2C* variants, including *CYP2C9*3*, which is known to reduce drug clearance, are important genetic factors related to phenytoin hypersensitivity including SJS/TEN.

The HLA association in drug reactions has a functional role in the pathogenesis. The reaction can be mediated by cytotoxic T lymphocytes in an HLA-restricted fashion. Granulysin produced by cytotoxic T lymphocytes or natural killer cells is a key mediator in the cytotoxic pathways of SJS/TEN.

Learning points:

The recent advances in pharmacogenomics and immune mechanisms of drug reactions have provided the foundation for personalised medicine in the near future.

Updates on contact dermatitis

Speaker: Chee-leok Goh
National Skin Centre, Singapore

Contact dermatitis is the commonest occupational skin disease. Chromate in cement is the commonest occupational allergen among construction workers in most parts of the world including Asia. In Europe, the incidence of chromate dermatitis from cement has decreased due to legislative measures that lowered the hexavalent chromate contents in cement. In developing countries, the cost-effectiveness of preventive measures against cement dermatitis must be considered against the background of generally lower labour costs and poor workers' compensation laws.

Besides, public health intervention was shown to reduce the prevalence of nickel allergy. The Danish government began to regulate consumer nickel exposure in 1990 due to the rising nickel allergy problem. The prevalence of nickel allergy in young Danish women decreased significantly after nickel regulation.

Recent reports of epidemics of contact allergy to preservatives and fragrance, especially a recent increasing prevalence of methylchoroisothiazolinone/methylisothiazolinone (MCI/MI) contact dermatitis from skin care products and industrial sources is a cause for concern that may require more proactive actions.

There is a need to develop a system to monitor environmental allergens that have the potential to cause epidemics. It is important to increase the awareness of contact dermatitis among workers and healthcare professionals, so that early investigation and treatment can be offered to affected workers. Moreover, effective preventative measures should be introduced to reduce morbidity and improve working capacity.

Learning points:

Public health intervention is important in the prevention of contact dermatitis among the workers and the general populations and workers.

Review of rare classical sexually transmitted disease

Speaker: Gang-yang Li
Guangdong Provincial Center for STI & Skin Disease Control, China

Cases of rare classical sexually transmitted diseases were presented. The first case was a gentleman with perineal verruca and palmar erythema. The diagnosis was condylomata lata which is commonly found in warm moist areas of the body and adjacent to the primary chancre of the perineum.

The second case was a neonate with congenital syphilis presenting with hypopigmented patches, erythema and blisters on the body. There was also hepatosplenomegaly, anaemia and radiological findings of periostitis. The adverse outcomes of syphilis in pregnancy include early foetal loss or stillbirth, prematurity, low birth weight and congenital syphilis. The outcome depended on the length of time since the mother was infected, VDRL titre and the gestational age at treatment. According to Centers for Disease Control and Prevention, US, the diagnosis of congenital syphilis is made by 1. an abnormal physical examination that is consistent with congenital syphilis or 2. a serum quantitative non-treponemal serological titre that is fourfold higher than the mother's titre or 3. a positive darkfield test or PCR of lesions or body.

The last case was periurethral swelling. The most common microbial causes are Gram negative bacteria, *Neisseria gonorrhoea* and *E. coli*.

Learning points:

Sexually transmitted diseases may present with a variety of dermatological symptoms. STI should be considered in the differential diagnosis.

HPV related anal dysplasia

Speaker: Chi-keung Kwan
Social Hygiene Service, Department of Health, Hong Kong

Anal dysplasia is a pre-cancerous condition. Anal dysplasia can progress from low grade changes to high grade changes and then progress to malignancy. There are more than 100 genotypes of human papillomavirus (HPV), while more than 40 HPV genotypes can infect the genital areas of males and females. The HPV causing anal dysplasia are mainly genotypes 6, 16, 18, 31, 53, 58.

Risk factors of anal dysplasia include exposure to HPV, multiple sexual partners, anal intercourse, HIV/AIDS infection, history of anal warts, history of sexually transmitted illness, immunosuppression and smoking.

Symptoms of anal dysplasia are non-specific, for example anal pain, pruritus and bleeding. However, the majority of anal dysplasia are asymptomatic. There is no common consensus among international organisations as to when to screen for anal dysplasia. A method of screening is anal Pap Smear. The Bethesda Criteria of Anal Pap Smear also categorises lesions into normal, ASCUS, ASCUSH, LGSIL, HGSIL . Patients with abnormal cytology should be referred for High Resolution Anoscopy (HRA) examination and biopsy if indicated. Any ulceration, erosion, irregular vascular patterns or aceto-white area shown in HRA should be considered for biopsy.

Learning points:

There are currently no national recommendations for screening anal dysplasia. History taking and physical examination are important. Dermatologists should be on the alert for anal symptoms and a history of cervical or vulvar dysplasia, HIV status, smoking, immunosuppression, and high-risk sexual practices, specifically receptive anal intercourse.