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# Updates on Autoimmune and Immunologically-mediated Dermatoses

## Dr. LY Chong

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**Editor**

Dr. LY Chong

In this issue, the main theme is focused on autoimmune and immunologically medicated dermatoses. The authors have given us updates on these potentially serious and life-threatening diseases, either primary cutaneous diseases with systemic complications or internal diseases with cutaneous manifestations. The cutaneous signs of these diseases often help the physicians in early diagnosis, monitoring of disease activities or prediction of the prognosis. Hopefully readers will agree that dermatology can be more than the skin's depth, and not just confined to cosmetic issues as often falsely impressed nowadays.

In the article of updates on lupus erythematosus, dermatomyositis & systemic sclerosis by Dr. RCW Su, the author has given a review on these three important and relatively common rheumatological diseases. These three systemic diseases are well known for their characteristic cutaneous manifestations. Some of these signs are almost pathognomonic of the disease, while the others are indicators of disease activity. Current classifications, diagnostic criteria and modern therapeutic options of these three diseases are covered in the article.

With the advances in laboratory methods, such as immunohistochemical study, immuno-electron microscopy, molecular technology, etc, more understanding is acquired in the pathogenesis of immunologically mediated diseases, and these new discoveries subsequently lead to the development of many new diagnostic or therapeutic tools. These can be vividly illustrated in the other two articles in the Medical Bulletin.

In the article on clinical features and diagnosis of common autoimmune bullous diseases in Hong Kong, Dr. PT Chan has given a detailed review on current thoughts in immuno-pathogenesis of pemphigus and pemphigoid. With the discovery of the target antigens of pemphigus (desmoglein I and II) by immunochemical methods, such as immunoprecipitation and immunoblotting, and the localisation of these antigens to the desmosomes by immunoelectron microscopy, vast advances have been achieved in understanding the pathogenesis of these diseases. The desmoglein compensation theory helps to explain for localisation of blisters at different sites in mucosal dominated type of pemphigus, mucocutaneous type of pemphigus and pemphigus foliaceus, thus clarify the enigma in these diseases that exists for decades. In addition, the discovery also leads to the development of new diagnostic tools like ELISA kits for measuring desmoglein 1 and 3. Similarly is the development of separate ELISA kits for BP180 and BP230 in bullous pemphigoid. These tools have the potential to improve the accuracy in diagnosis and monitoring of the disease activities.

With emerging of the new concepts about erythema multiforme, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), classification of these diseases have been totally revised. The old concept that Stevens-Johnson syndrome is a major form of erythema multiforme is now obsolete, while the former is now classified in the same spectrum of toxic epidermal necrolysis. A new model has been proposed to explain the pathogenesis of SJS-TEN with the Fas signalling pathway, leading to apoptotic cell death in this spectrum of

diseases. In the article by Dr. HHF Ho, a comprehensive review of SJS-TEN has been given, together with a pragmatic approach in the management of these two serious diseases, which often are managed by multidisciplinary teams including dermatologists, internists, ophthalmologists and paramedical personnel.

In line with the main theme of this issue, Dr. CK Yeung has reviewed the current applications of intravenous immunoglobulin (IVIg) in immunologically related dermatoses. One of the important indications of IVIg with proven value is TEN. It is now believed that in SJS-TEN, Fas ligand is upgraded and expressed on the keratinocyte surface, leading to apoptosis and cell death via Fas-FasL interaction. IVIg blocks the Fas receptor, thus inhibits the formation of Fas-FasL complex and prevents further apoptosis. Besides this indication, IVIg has been studied in a wide range of other serious dermatological conditions as mentioned in this article.

After attending the 66th Annual Meeting of the American Academy of Dermatology, Dr. FC Ip has given us a brief report on the session of Update on Paediatric Dermatoses, a subspecialty which is still not well-developed in Hong Kong. The author has reported on two important paediatric diseases, namely atopic dermatitis and Kawasaki's disease. New current concepts about the pathogenesis and new therapeutic issues have been mentioned for readers' awareness and watch out.

Finally, as usual, a non-medical article has been included to pursue the tranquillity of mind. Dr. CK Kwan, an experienced hiker, has entertained us about the pleasure and interesting routes of hiking in Hong Kong. Hopefully, apart from chasing various targets in our medical career, all of us could develop some healthy hobbies in our life.

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# Update on Lupus Erythematosus, Dermatomyositis & Systemic Sclerosis

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*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 one CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 31 October 2008.*

## Lupus Erythematosus

In the 19th century, a group of diseases of erythematous and atrophic nature was classified as lupus erythematosus (LE). It was thought that the skin appearance was due to the gnawing by a wolf (Latin: lupus). Cutaneous lesions of LE may be associated with significant internal abnormalities in systemic LE (SLE). (Table 1)

Gilliam divided cutaneous lesions of LE into those that show characteristic histopathological changes of LE (LE-specific skin disease or cutaneous LE) and those that are not histopathologically distinct for LE and also seen in other conditions (LE-nonspecific skin disease).

Cutaneous LE is further subdivided into acute cutaneous LE (ACLE), subacute cutaneous LE (SCLE), and chronic cutaneous LE (CCLE). This is related to the pace and severity of any associated SLE more than how long individual lesions have been present. ACLE always occurs in the setting of acute flaring SLE with visceral involvement. SCLE patients meet SLE criteria about 50% of the time. CCLE patients often have skin only or skin predominant disease, occurring in absence of SLE or in presence of smouldering SLE. Cutaneous LE is also defined in part histopathologically by the location and depth of inflammatory infiltrate.

## Cutaneous Manifestations of SLE

LE-nonspecific skin lesions include non-scarring alopecia, mouth ulcers, photosensitivity, Raynaud's phenomenon, and vasculitis/vasculopathy. They are a marker of underlying systemic disease activity and often herald a flare of SLE.

In a recent study of cutaneous manifestations of SLE patients from Chinese patients in HK, telogen effluvium (27.8%), Raynaud's phenomenon 14.8%, periungal telangiectasia (13%), and urticaria or urticarial vasculitis (9.6%) were the most common LE-nonspecific skin disease at interview. Localiszed ACLE (38.3%), SCLE (9.6%), and discoid LE (9.6%) were the most common LE-specific skin disease.[1]

One local study found that 17% of patients with discoid LE subsequently develop SLE.[2] Another local survey revealed that SLE patients with cutaneous components constituted one third of newly diagnosed LE patients seen in dermatology clinics of public service. SCLE and discoid LE each constitute one third of the newly diagnosed LE.[3]

## Management of Cutaneous LE

Patients should be advised to avoid mid-day sun. Protective clothing and broad spectrum sunscreens that shield out UVA and UVB are required. The sunscreen should have sun protection factor (SPF) >15. Frequent applications of sunscreens are necessary, especially at the time of profuse sweating and swimming. Drugs that potentially aggravate LE should be avoided. Hydrochlorthiazide, calcium channel blockers, and angiotensin converting enzyme inhibitors (ACEI) have been implicated in drug-induced SCLE.

## Topical Therapy

Topical treatment includes potent topical or intralesional steroid for localiszed and mild disease. Mild steroid is sufficient for neonatal lupus erythematosus. Care should be exercised to avoid side effects induced by prolonged application, especially on the face. Potent topical steroid application should be restricted only to areas of active inflammation.

Topical tacrolimus and pimecrolimus are effective in treatment of cutaneous LE. Although probably not as effective as superpotent topical steroids, they have a role when cutaneous atrophy, either disease or treatment related, is a concern.

## Systemic Therapy

Antimalarials, such as hydroxychloroquine are effective for skin and joint involvements. It is used for widespread cutaneous diseases and may prevent new eruptions. The initial dose is 400mg/day, followed by 200-400mg/day depending on response. Response usually occurs in 4-6 weeks. The risks of retinal toxicity should be discussed with the patient, and the anti-malarial needs to be discontinued if this occurs. The risk

of antimalarial retinopathy is rare if the daily dose of hydroxychloroquine is <6.5mg/kg/day, based on ideal body weight. Complete blood picture, renal and liver function should be monitored and regular examinations by an ophthalmologist is required before and every 6-12 months while on therapy. If the response to hydroxychloroquine is poor, quinacrine may be tried, but yellowish skin discoloration is a notable side effect. (Table 2)

Before considering patients who failed to respond to an adequate trial of antimalarial therapy as antimalarial refractory, one should check for sun-protection, compliance with therapy, review the diagnosis and assess for possibility of lichenoid drug eruption. Antimalarial refractory cutaneous lupus may be treated with systemic retinoids and dapsone. Systemic retinoids are useful for hyperkeratotic discoid LE lesions but are teratogenic. Dapsone is effective for bullous SLE, vasculitis, oral ulcerations and sometimes discoid LE. Haemolytic anaemia is a major side-effect and it should not be used in patients who have G6PD deficiency.

Thalidomide is an alternative when antimalarial fails. It is teratogenic and contraindicated in women of child bearing age. Neuropathy is an important side effect, and patients should receive periodic neurologic assessments and nerve conduction studies. Other treatments that have been reported useful in cutaneous LE include oral gold, clofazimine and sulphasalazine.

Systemic steroid is very useful for treatment of systemic disease and refractory skin disease. However side-effects limit its prolonged use. Immunosuppressive agents such as azathioprine are most commonly given with prednisolone as a steroid-sparing agent. Other cytotoxic agents used include methotrexate, mycophenolate, and cyclophosphamide.

Experimental therapies for therapy-resistant cutaneous lupus include immunomodulatory agents such as intravenous immune globulin (IVIg), anti-CD4 monoclonal antibody infusion and interferon-alpha 2a.[4] The use of interferon-alpha may be counter-intuitive as recent data suggest that interferon-alpha may induce SLE. The choice of therapy for antimalarial refractory cutaneous lupus depends on the evaluation of risk to benefit ratio for each individual patient.

## Dermatomyositis

Dermatomyositis (DM) is characterised by a specific skin rash and muscle inflammation with weakness. In addition to skin and skeletal muscle involvements there may be involvement of gastrointestinal system, heart and lung. These may lead to dysphagia, aspiration, cardiomyopathy, arrhythmias and pulmonary fibrosis.

The characteristic skin eruption consists of Gottron's papules over knuckles and heliotrope rash on eyelids. There may be violaceous erythema in photodistribution and periungal changes. Muscle involvement leads to muscle pain and tenderness affecting limb girdle and proximal limbs. Muscle weakness is symmetrical and bilateral. Facial and bulbar muscles may be affected. Investigations are performed for making diagnosis, assessing muscle disease, underlying aetiology (malignancy or auto-immune screen), and systemic (pulmonary, oesophageal and cardiac) involvement.[5]

## Malignancy Associated Dermatomyositis

Malignancy occurs with adult onset DM, especially >40 years old. There are often constitutional symptoms, rapid onset of DM, and lack of Raynaud's phenomenon. All adult DM patients should be evaluated for underlying malignancy, and extent depends on the clinical findings. The risk of malignancy is significant within the first two years of diagnosis of DM. Common malignancies reported include breast, lung, gastro-intestinal and ovarian cancer. In our locality, nasopharyngeal carcinoma is the most common association. Removal or treatment of the underlying malignancy may be associated with resolution of DM, and recurrence of malignancy may lead to relapse of DM.

## Dermatomyositis Associated with Autoimmune Connective Tissue Disease

Dermatomyositis/polymyositis may overlap with other connective tissue diseases. This condition characteristically affects young females. Sclerodermatous changes are most frequently observed and known as sclerodermatomyositis. Antibodies anti-Ku and anti-PM/scl may be present. Mixed connective tissue disease (associated with high anti-ribonucleoprotein RNP), rheumatoid arthritis, lupus erythematosus, and Sjogren's syndrome may occur concomitantly. DM associated with interstitial lung disease is frequently the cause of death. Anti-Jo1 antibody correlates with development of pulmonary disease.

## Amyopathic Dermatomyositis

Classic DM may present with preceding skin disease before evidence of muscle disease. Amyopathic DM patients have characteristic skin disease in the absence of muscle disease for over 6 months.

Clinically amyopathic DM (CADM) also includes characteristic skin disease without muscle weakness but with subclinical evidence of myositis in laboratory, electrophysiological and radiological (MRI) evaluation. Follow up of CADM revealed that they may develop late onset muscle weakness, interstitial lung disease, and malignancy. Local studies have shown a strong association between adult CADM patients and nasopharyngeal carcinoma, therefore these patients should be evaluated for malignancy in the same way as in adult classic DM. [6]

## Childhood Dermatomyositis

They usually have slow progressive weakness with calcinosis of the intermuscular fascial planes.

Calcinosis may also be subcutaneous and acral (elbow, knees and fingers) as in adults. Childhood DM is usually steroid responsive, but associated with contractures and deformity leading to functional disability. One unusual form of childhood DM is characterised by vasculitis of muscles and gastrointestinal tract, rapid onset of severe weakness, steroid unresponsiveness and high mortality. Internal malignancy is usually absent in childhood DM.

## Treatment

Successful treatment of underlying malignancy leads to resolution of malignancy associated DM.

There is little correlation between skin and muscle disease activity in DM. For skin disease, sun protection, topical steroids and antimalarials are the mainstay of treatment. Sun-protection involves avoiding outdoor activity around mid-day, protective clothing, broad spectrum UVA and UVB sunscreens with SPF >15. Anti-malarial therapy consists of hydroxychloroquine (<6.5mg/kg/day) or chloroquine (<4mg/kg/day). Second line treatments include topical tacrolimus, methotrexate or mycophenolate.

For treatment of muscle involvement bed rest is required during the acute phase. Physiotherapy is especially important in juvenile dermatomyositis to prevent contractures and deformity. Systemic steroids and immunosuppressive agents are the mainstay of therapy for myositis. (Table 3) Initial dose of prednisolone is 1mg/kg/day with dose adjusted according to clinical response and muscle enzymes. The effect of other immunosuppressive agents is often delayed when compared with systemic steroids, but they have a steroid sparing effect. The most often used first-line immunosuppressive agents are methotrexate or azathioprine. Other immunosuppressive agents include mycophenolate, cyclophosphamide, chlorambucil and cyclosporine. Biologics against TNF-alpha, such as etanercept and infliximab, have been used successfully in a few patients that are refractory to conventional therapy. This supports a role for TNF-alpha in the pathogenesis of muscle inflammation in DM.

Plasmapheresis, intravenous (IV) pulse steroid, and intravenous immunoglobulin (IVIg) have been tried in acute life threatening stages for rapid control and stabilisation. High dose IVIg (2g/kg body weight) monthly for three months was found to be effective in a double blind, placebo controlled trial with significant improvement in muscle strength, neuromuscular symptoms and skin disease. Early aggressive therapy in juvenile dermatomyositis with IV pulse steroids is associated with lower incidence of disabling calcinosis cutis. Calcinosis cutis may respond to diltiazem and/or to surgical excision. Studies of therapy with rituximab (a CD20 B cell-depleting antibody) have provided encouraging results in patients who have not responded to other treatments.

Except for adult onset DM with advanced malignancy, the prognosis of treated DM in children and adults are relatively good. The major causes of mortality apart from advanced malignancy are pulmonary fibrosis or treatment complications.

## Systemic Sclerosis

Scleroderma describes the thickening and hardening of the skin due to progressive accumulation of dermal collagen, leading to fibrosis and loss of mobility of skin. It exists as cutaneous or systemic form.

Cutaneous scleroderma includes morphea, linear scleroderma and generalised morphea, which are confined to the skin as tight indurated plaques. Systemic scleroderma refers to multi-system disease with immune inflammation, vascular abnormalities and fibrosis. It is characterised not only by skin sclerosis and Raynaud's phenomenon, but with internal organ involvement and associated morbidity or even mortality. The course of the disease is defined by the extent of skin and internal organ involvement.

Limited systemic scleroderma (lSSc) has skin involvement limited to hands and feet, arms and legs distal to the elbows and knees, the face and neck. The course is indolent, internal organ involvement may not appear for years and patients often die of other causes. There is a long history of preceding Raynaud's phenomenon and a high incidence of anti-centromere antibody. CREST syndrome is a variant of lSSc characterised by **C**alcinosis of finger tips, **R**aynaud's phenomenon, oesophageal dysmotility with dysphagia and reflux, **S**clerodactyly of hands and fingers, and matted **T**elangiectasia on face and hands.

Diffuse systemic scleroderma (dSSc) has a rapid onset and diffuse involvement affecting the entire skin surface with early onset of internal involvement. It is known as progressive systemic sclerosis and characterised by proximal sclerosis, sclerodactyly, digital pitting scars of finger tips or loss of substance of distal finger pad, and bilateral basilar pulmonary fibrosis. Apart from the skin, dSSc affects the lung, heart, kidney, and gut. Pulmonary hypertension and renal failure are the common causes of death. Anti-centromere antibodies are uncommon, but Scl-70 antibodies are present in 33% of cases.

## Treatment:

Many agents have been tried over the years, but no single agent has been found to reliably arrest or reverse the fibrosing process.

D-penicillamine was once thought to reverse the fibrosing process by interfering with cross-linking of collagen. However one study showed that D-penicillamine at low doses 125mg alternate day is as effective as high dose 750mg-1000mg daily and side effects were much reduced.[7] This raises questions about the therapeutic efficacy of D-penicillamine in treatment of systemic sclerosis.

Low dose prednisolone 20mg daily has been shown to reduce skin thickness scores. Methotrexate 15-25mg weekly shows significant improvement in skin induration and grip strength in a randomised double-blind trial.[8] However another randomised controlled trial failed to reproduce these findings.[9] It is also uncertain how improvement in skin scores is translated into clinical benefit and improvement in quality of life.

Oral cyclophosphamide (1-2mg/kg/day) plus oral prednisolone (40mg every other day) significantly improved skin score and prevented the development of lung fibrosis in a controlled study. Colchicine 0.5mg bd may be effective and well tolerated, however controlled trials are not available. Other therapies reported useful include UVA and UVA1 phototherapy.

Apart from attempting to reverse fibrosing process in skin, the aim of treatment is both symptomatic and to prevent complications where possible.

Raynaud's phenomenon and digital ischaemia should be managed by stop smoking, avoiding cold exposure and avoiding drugs such as beta-blockers. Drugs employed to treat Raynaud's phenomenon include nifedipine, a calcium channel blocker that reduces vasospasm and improve peripheral blood flow. Losartan, an angiotensin II receptor antagonist and intravenous iloprost (a prostacyclin analogue) were found to reduce the frequency and severity of Raynaud's phenomenon. This may be supplemented with pentoxifylline and antiplatelet agents such as aspirin, dipyridamole or clopidogrel. Topical nitrates and keeping hands warm with electrically heated gloves are also helpful.

Topical emollients have a role in prevention of skin breakdown. Cutaneous ulcers may be managed by protective occlusive dressing. Surgical hand repair has shown favourable results in alleviation of pain, prevention of tissue loss, preservation of hand function, and improvement in aesthetics. Physiotherapy should be performed with emphasis on range of motion of joints and mouth opening, to prevent contractures and deformity thereby preserving function.

Extra-cutaneous involvement such as renal hypertension, pulmonary hypertension and gastrointestinal symptoms should be managed with multidisciplinary team of specialists. Treating hypertension with ACEI helps to limit progression of renal disease. Renal transplantation may be considered for renal failure. Epoprostenol (prostacyclin derivative), bosentan (endothelial receptor antagonist), sildenafil (phosphodiesterase 5 inhibitor) may be used in the treatment of pulmonary hypertension to improve cardiopulmonary haemodynamics. Cyclophosphamide improves lung function outcome and survival in patients with alveolitis.[10] Sleeping upright, antacids, H2 antagonists, omeprazole and metoclopramide may be useful for oesophageal reflux. (Table 4)

Although there is still a high case specific mortality in progressive systemic sclerosis, there have been significant advances in the management of skin, renal and pulmonary complications.

*Table 1: Adapted from ACR 1982 revised criteria for classification of SLE*

| Criterion | Definition |
|---|---|
| 1. Malar rash | Fixed erythema, flat or raised, over the malar eminences, tending to spare nasolabial fold. |
| 2. Discoid rash | Erythematous raised patches with adherent keratotic scaling and follicular plugging , atrophic scarring may occur in older lesions |
| 3. Photosensitivity | Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation |
| 4. Oral ulcers | Oral or nasopharyngeal ulceration, usually painless, observed by a physician |
| 5. Arthritis | Nonerosive arthritis involving 2 or more peripheral joints, characterisized by tenderness, swelling or effusion |
| 6. Serositis | Pleuritis<br>Pericarditis |
| 7. Renal disorder | Persistent proteinuria<br>Cellular casts- |
| 8. Neurological disorder | Seizures<br>Psychosis |
| 9. Haematological disorder | Haemolytic anaemia<br>Leukopenia<br>Lymphopenia<br>Thrombocytopenia |
| 10. Immunological disorder | Positive LE cell preparation OR<br>Anti-DNA<br>Anti-Sm<br>False positive serological test for syphilis |
| 11. Anti-nuclear antibody | An abnormal titre of anti-nuclear antibody in the absence of drugs known to be associated with drug-induced lupus. |

ACR- American College of Rheumatology
A person is said to have SLE if ≥4 of 11 criteria are present, serially or simultaneously.
# Update Diagnostic & Therapeutic Criteria Committee of ACR 1997: For immunological disorders, delete positive LE cell preparation and add detection of lupus anticoagulant or abnormal serum level of IgG or IgM anti-cardiolipin antibodies.

*Table 2: Therapy for Cutaneous LE*

| |
|---|
| **Local therapy** |
| Sun-protection (2) |
| Topical or intralesional steroid (2) |
| Topical tacrolimus or pimecrolimus (2) |
| **Systemic anti-malarial therapy** |
| Hydroxychloroquine 200-400mg qd (<6.5mg/kg) (2) |
| Chloroquine 125-250mg qd (<4mg/kg) (2) |
| Quinacrine 100mg qd (2) |
| Combination of hydroxychloroquine/chloroquine + quinacrine (2) |
| * Encourage discontinuation of smoking |
| **Systemic therapy for anti-malarial resistant cases** |
| Retinoids (2) |
| Dapsone (2) |
| Thalidomide (2) |
| Gold (2) |
| Clofazimine (3) |
| Sulphasalazine (2) |
| Azathioprine (2) |
| Systemic steroids (3) |
| IVIg, anti-CD4 monoclonal antibody, interferon-alpha 2a (3) |
| (1) Prospective control trial |
| (2) Retrospective study or large case series |
| (3) Small case series or individual case reports |

*Table 3: Therapeutic options for Dermatomyositis*

| | Cutaneous Disease | Muscle Disease |
|---|---|---|
| First Line | sun-protection (3)<br>topical steroid (3)<br>antimalarials (2) | prednisolone (2)<br>methotrexate (2)<br>azathioprine (3) |
| Second Line | topical tacrolimus (3)<br>methotrexate (2),<br>mycophenolate (3) | cyclophosphamide (2),<br>chlorambucil (2)<br>mycophenolate (2),<br>cyclosporine (2) |
| Third Line | intravenous immunoglobulin (1)<br>intravenous pulse steroids (3)<br>etanercept (3), infliximab (3), rituximab (2) | |

(1) Prospective control trial
(2) Retrospective study or large case series
(3) Small case series or individual case reports

*Table 4: Therapeutic options for systemic sclerosis*

| Skin fibrosis Scleroderma | Raynaud's phenomenon | Extracutaneous complications | | |
|---|---|---|---|---|
| | | Pulmonary Hypertension | Hypertension & renal crisis | Oesophageal reflux |
| penicillamine<br>methotrexate<br>prednisolone<br>cyclophospha-mide<br>colchicine<br>UVA | nifedipine<br>losarten<br>iloprost<br>aspirin<br>clopidogrel<br>pentoxifylline | epoprostenol<br>bosentan<br>sildenafil<br>**Lung Fibrosis**<br>cyclophosphamide | ACEI<br>renal transplant | antacids<br>H2 antagonists<br>omeprazole<br>metoclopromide |

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## MCHK CME Programme Self-assessment Questions

**Please read the article entitled "Update on Lupus Erythematosus, Dermatomyositis & Systemic Sclerosis" by Dr. RCW Su, and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded 1 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 October 2008. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.**

**Questions 1-10: Please choose the best answer.**

**1. The most common cutaneous LE (LE specific lesion) in SLE is:**
A. non-scarring alopecia
B. mouth ulcers
C. Localised ACLE / malar rash
D. Raynaud's phenomenon
E. vasculitis/vasculopathy

**2. ACR revised diagnostic criteria for SLE do not include:**
A. photosensitivity
B. malar rash
C. haemolytic anaemia
D. lupus anticoagulant/anticardiolipin antibodies
E. cardiomyopathy

**3. The following are recognised therapeutic agents for cutaneous LE except:**
A. topical or intralesional steroid
B. antimalarials
C. dapsone
D. penicillamine
E. thalidomide

**4. Pulmonary fibrosis may complicate dermatomyositis in association with:**
A. Anti-Jo1 antibodies
B. Anti-RNP antibodies
C. Anti-Centromere antibodies
D. Anti-Scl antibodies
E. Anti-Ro antibodies

**5. The following may be features of clinically amyopathic dermatomyositis except:**
A. elevated levels of muscle enzymes
B. abnormal EMG changes
C. MRI changes of muscle disease
D. muscle weakness <6 months from onset of characteristic skin disease
E. associated underlying malignancy such as nasopharyngeal carcinoma

**6. Which of the following is not a treatment for dermatomyositis:**
A. treatment of associated underlying malignancy
B. nifedipine
C. systemic steroids
D. methotrexate
E. intravenous immunoglobulin IVIg

**7. The most characteristic feature of progressive systemic sclerosis is:**
A. calcinosis
B. Raynaud's phenomenon
C. early onset progressive internal organ involvement
D. sclerodactyly
E. telangiectasia on face and hands

**8. The following agents have been used in treating scleroderma except:**
A. bleomycin
B. colchicine
C. methotrexate
D. cyclophosphamide
E. prednisolone

**9. Raynaud's phenomenon in systemic scleroderma is aggravated by:**
A. calcium channel blockers
B. beta-blockers
C. angiotensin II receptor antagonists
D. ACE inhibitors
E. intravenous iloprost

**10. Pulmonary hypertension in systemic sclerosis may be treated with:**
A. systemic steroids
B. methotrexate
C. cyclophosphamide
D. nifedipine
E. epoprostenol

## ANSWER SHEET FOR OCTOBER 2008

**Please return the completed answer sheet to the Federation Secretariat on or before 31 October 2008 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.**

# Update on Lupus Erythematosus, Dermatomyositis & Systemic Sclerosis

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

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**Update on Treatment of Osteoporosis**

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

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# Clinical Features and Diagnosis of Common Autoimmune Bullous Diseases in Hong Kong

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Dr. PT Chan

## The Spectrum of Autoimmune Bullous Diseases

Autoimmune bullous diseases are a group of cutaneous disorders characterised by skin blistering or erosions as a result of development of autoimmunity. It can be classified according to the anatomical sites of blister into two types: intraepithelial and subepidermal. It can be subdivided further according to the clinical features, type and location of immunoreactants found on skin biopsy (Table 1 and 2). The term "pemphigus" refers to intraepithelial blistering skin diseases. The term "pemphigoid" refers to blistering diseases occurring at the dermo-epidermal junction in general, although not every subepidermal bullous disease bears the term "pemphigoid" in the nomenclature (Table 2). With extensive research, most of the target antigens of these disorders have been characterised. It is amazing to see that earlier disease classification by clinical features and pathological findings alone did have a molecular basis, as distinct antigens are targets for different entities in most of the subgroup of autoimmune bullous diseases. The antigens of pemphigus are found in desmosomes between keratinocytes, which are organelles mediating intercellular adhesion together with tissue morphogenesis and differentiation. On the other hand, the antigens of subepidermal bullous diseases are found in the basement membrane zone at the dermo-epidermal junction. Research in these target antigens has led to a better understanding of their biologic functions, advance in disease diagnosis, monitoring of disease activity, and can be potentially employed for antigen specific therapy.

*Table 1. Classification of major autoimmune intraepithelial bullous diseases and their target antigens*

| | Target antigen(s) |
|---|---|
| Pemphigus foliaceus | Desmoglein 1 |
| Pemphigus vulgaris | Mucosal pemphigus vulgaris: Desmoglein 3<br>Mucocutaneous pemphigus vulgaris: Desmoglein 3 and 1 |
| IgA pemphigus | Subcorneal pustular dermatosis type: Desmocollin 1<br>Intraepidermal neutrophilic type: Unknown |
| Paraneoplastic pemphigus | Desmogleins 1 and 3, Plakins, 170kD unknown antigen |

*Table 2. Classification of major autoimmune subepidermal bullous diseases and their target antigens*

| | Target antigen(s) |
|---|---|
| Bullous pemphigoid | BP180, BP230 |
| Pemphigoid gestationis | BP180, BP230 |
| Linear IgA bullous dermatosis | BP180 |
| Epidermolysis bullosa acquisita | Collagen VII |
| Bullous lupus erythematosus | Collagen VII |
| Cicatricial pemphigoid | BP180, laminin, $\alpha_4$ and $\beta_6$ subunits of integrin |

## Epidemiology of Autoimmune Bullous Diseases in Hong Kong

Autoimmune bullous diseases are uncommon in Hong Kong. In a local retrospective survey done in Social Hygiene Service in Hong Kong between 1985 and 1992, 234 Chinese patients were diagnosed by skin biopsies to have autoimmune bullous diseases.[1] Bullous pemphigoid (BP), pemphigus vulgaris (PV) and pemphigus foliaceus (PF) were the three most common autoimmune bullous diseases in Hong Kong and they accounted for 63.7%, 16.2% and 9.9% of cases respectively. BP tended to occur in the elderly whereas PV and PF affected patients with slightly younger ages. The mean age of presentation of BP patients was 70 year (standard deviation (SD) 15) and those for PV and PF were 57 year (SD 14) and 63 year (SD 13) respectively. These three entities are also the most characterised ones and the on going discussion will be concentrated on them.

## Pemphigus Foliaceus

It can be divided into two major forms: sporadic and endemic types, although occasionally drug-induced PF is also seen. These two major forms have similar clinical lesions. Endemic PF is found in rural areas of Brazil, Columbia and Tunisia where clustering along rivers, within the same family, occurrence at young age and association with insect bite are observed.[2] Endemic PF provides an interesting model where an autoimmune disease arises as a result of interplay of genetic and environmental factors and there are dozens of papers published in this regard. PF manifests as cutaneous erosions. Intact blisters are less commonly found as the level of splitting is intraepidermal. Thus the roof of the blisters is relatively thin and easily ruptures. These erosions are commonly found in seborrhoeic areas, like the face, upper chest and back. Erythrodermic cases are sometimes seen, mainly in

patients suffering from endemic PF. Oral and mucosal erosions are not found in PF. The skin fragility in PF patients is demonstrated by the Nikolskiy sign. This sign indicates the ability to remove the superficial skin by pulling the edge of the cutaneous erosion or rubbing at the lesion edge and/or rubbing clinically the normal skin distant from the cutaneous erosions. There are variations of the tests such as the Asboe-Hansen sign; but these signs are not 100% specific as they only indicate skin fragility and can be found in other disorders as well, e.g. bullous pemphigoid, linear IgA bullous dermatosis and staphylococcal scalded skin syndrome.[3]

## Pemphigus Vulgaris

PV, as opposed to PF, does have oral/ mucosal erosions. Similar to PF, as the roof of the blisters is thin, intact blisters are less commonly seen. It can be divided into two stages: mucosal PV and mucocutaneous PV. Patients with PV often presents initially as oral erosions, although other mucosal surfaces can also be involved (mucosal PV). About half of the patients will develop cutaneous erosions subsequently in addition to mucosal erosions (mucocutaneous PV). In severe forms, both PF and PV can disrupt the epidermal barrier leading to dehydration, electrolyte imbalance, temperature dysregulation, sepsis and can be life-threatening. Nikolskiy sign is also positive in PV.

## Desmoglein: The Target Antigen in PF and PV

***Desmoglein 1 as a common target in PF and staphylococcal scalded skin syndrome***

The target of autoimmunity in PF is desmoglein 1. It is a transmembrane glycoprotein located in the desmosomes. Desmoglein 1 is mostly found in the subcorneal layer of the epidermis and this is the level of split observed on histopathology (see Diagnosis of autoimmune bullous diseases). Similar subcorneal splitting in the epidermis is also observed in staphylococcal scalded skin syndrome and bullous impetigo. The reasons of their similarity remained puzzle for a long time until it was found out that the exfoliative toxin of *Staphylococcus aureus* was a serine protease that cleaved desmoglein 1. Thus, both PF and staphylococcal scalded skin syndrome are diseases secondary to loss of desmoglein 1 function by autoantibodies and bacterial enzymes respectively.[4] On body surface, most desmoglein 1 is localised in the seborrhoeic areas where PF lesions are often found.[5]

***Desmoglein compensation hypothesis***

The autoimmune target of mucosal PV is desmoglein 3. It is hypothesised that the phenomenon of epitope spreading occurs subsequently, leading to the development of autoimmunity to both desmogleins 1 and 3 in mucocutaneous PV. Subsequent in vivo studies have shown that desmogleins can compensate for the function of each other.[4] In normal human epidermis, desmoglein 1 is expressed mainly on the subcorneal layer, with some extension below to suprabasal areas; whereas desmoglein 3 is mainly expressed on the suprabasal layers, not extending to subcorneal layers. Thus in PF, the loss of desmoglein 1 function by anti-desmoglein 1 antibodies would lead to subcorneal splitting on skin surface, where only desmoglein 1 is found.

In normal human mucosa, desmoglein 1 is also expressed subcorneally and desmoglein 3 is expressed mostly suprabasally. In contrast with skin epithelium, the expression of desmoglein 3 extends to the subcorneal layer in mucosal areas and desmoglein 1 expression is only limited to subcorneal layers without further extension. In PF, no mucosal lesions are observed as the presence of desmoglein 3 across the entire mucosal epithelium compensates for loss of desmoglein 1 function.

In mucosal PV, where anti-desmoglein 3 antibodies are found, suprabasal splitting occurs at mucosal surface only as this site only expresses desmoglein 3 without desmoglein 1. In skin epithelium, the presence of some desmoglein 1 in suprabasal layers compensates for loss of function of desmoglein 3 and no skin blistering is observed. But when anti-desmoglein 1 and 3 antibodies are present in mucocutaneous PV, suprabasal blisters occur both in the mucosa and skin surface. This hypothesis is a good model illustrating how basic science can help physicians to understand the pathophysiological basis of clinical disease phenotype observed in their practice.[6]

## Bullous Pemphigoid - Clinical Features and its Immune Target

BP is the most common autoimmune bullous diseases in Hong Kong. It often affects elderly patients. Patients with BP typically present as intact blisters as the roof of blister, which is comprised of the entire epithelium, is thicker than that in pemphigus. The blister size ranges from small to large and can develop on erythematous, urticarial or even normal looking skin. Blister fluid can be clear or haemorrhagic. These blisters are most commonly found over the flexural areas of skin surface, such as the abdomen, inner thighs, groins or axillae but they can occur everywhere. Classically, no scarring or milia are seen in BP, as opposed to diseases affecting deeper part of dermo-epidermal junction such as epidermolysis bullosa acquisita. Mucosal surfaces are affected in 10-40% of cases. But as buccal cavity is a confined space, blisters readily rupture in this area and erosions are seen instead. Usually patients with BP suffer from intense pruritus. Sometimes patients with BP present atypically as pruritic nodules (pemphigoid nodularis), localised blisters over palms or soles (dyshidrotic BP), figurate urticarial lesions or vulval erosions especially in children. A high index of suspicion is required for diagnosing these atypical BP.

The target antigens of BP are BP180 and BP230.[7] BP180 is a transmembrane protein found in the lamina lucida of the basement membrane zone. BP180 is a large molecule and within the molecule, an extracellular non-collagenous domain, NC16a, is found to be an important autoimmune epitope in BP. On the other hand, BP230 is a molecule located intracellularly in hemidesmosomes, an organelle important for adhesion of basal cells to basement membrane. Thus the site of detachment in BP is at the basement membrane and subepidermal blister is found on histology (see Diagnosis of autoimmune bullous diseases).

## Diagnosis of Autoimmune Bullous Diseases

The diagnosis of autoimmune bullous disease requires clinico-pathological correlation. An exhaustive list of differential diagnosis of skin blisters or erosions is beyond the scope of this short review, but potential ones include inherited epidermolysis bullosa, herpes simplex/ zoster, staphylococcal scalded skin syndrome, bullous impetigo, lichen planus pemphigoides, scald injury, fixed drug eruption, toxic epidermal necrolysis, porphyria cutanea tarda, diabetic bullae, pseudoporphyria, etc. It is essential to perform skin biopsy for histopathology and direct immunofluorescence test (DIF) to establish a firm diagnosis, bearing in mind that the treatment of these diseases often requires long term treatment with immunosuppressant.

In PV and PF, the core features include intraepithelial blisters/ split, acantholysis (which signifies loss of cellular adhesion) and variable underlying dermal inflammatory infiltrate. In PF, the split is more superficial (subcorneal) whereas in PV, the split is deeper down (suprabasal). In BP, subepidermal blisters are observed and the typical inflammatory infiltrate is predominantly eosinophilic. Besides, secondary changes such as scale crust formation or re-epithelialisation may be present depending on the stage of evolution.

## Direct Immunofluorescence Test

DIF detects immunoreactants present on biopsied tissues and by definition all autoimmune diseases should have positive DIF to immunoglobulin. However, occasionally, errors in choosing the biopsy site, previous treatment with topical or oral steroid or delay in transport of specimen may lead to false negative. In PF/ PV, the IgG are bound to keratinocyte intercellular surfaces, while in BP, IgG are bound to the basement membrane zone as a linear band. Complement is found in almost all BP cases and may be variably found in PV or PF on DIF.

## Indirect Immunofluorescence Test

The historical landmark finding of the presence of circulating anti-skin antibodies in sera of pemphigus patients first defined it as an autoimmune disease.[8] Then it was observed that titre of anti-skin antibodies correlates with disease activity in pemphigus, but not in BP.[9] Titre of anti-skin antibodies is conventionally estimated by the indirect immunofluorescence test (IIF). The basic principle of this test is to determine the highest sera dilution that can still give a positive intercellular surface (in PV or PF) / linear basement membrane (in BP) staining pattern on a predefined epithelial substrate as determined by immunofluorescence microscopy. The titres are often represented as multiples of a fraction, like 1/10, 1/40 or 1/160. However, the test is both operator and substrate dependent.

With the identification of target antigen and advancement of molecular biology, these antigens can be produced and purified in vivo. Now commercial ELISA kits are available for measuring desmoglein 1 and 3 reactivity.[10] Besides being sensitive and specific, these ELISA kits have several advantages over the conventional IIF in that they are more objective, antibody titre is represented by continuous valuables and they are not substrate dependent. Desmoglein 1 and 3 ELISA indexes have been proven to correlate well with disease activity in PF and PV. The titre of antibody in BP, as measured by IIF, does not correlate with disease activity. By the development of separate ELISA kits for BP180 and BP230, it has been found out that ELISA BP180 index does correlate with disease activity but ELISA BP230 index only sometimes fluctuates with change in disease activity.[7, 11] As titre of antibodies measured by IIF represents both anti-BP180 and anti-BP230 activities, it explains why older studies have failed to demonstrate a relationship between antibody titre and disease activity in BP.

ELISA tests reflect the amount of antibodies in patients' sera but not the presence of antibodies bound to skin of the patients. To diagnose immunobullous disease by skin biopsy, besides the level of splitting/ blister, we aim at finding the presence of tissue bound immunoglobulin by DIF as a circumstantial proof of its aetiology of skin blistering. There is some degree of overlap of desmoglein 1 and 3 ELISA indexes in pemphigus patients with those in patients suffering from BP and other connective tissue diseases, especially at marginally elevated ELISA indexes.[12] Moreover, commercial ELISA kits are not available for some antigens of autoimmune bullous skin diseases, such as desmocollin 1 and plakins. Thus, ELISA test cannot replace DIF completely as a diagnostic test of autoimmune bullous diseases.

## Conclusion

In summary, BP, PV and PF are the three most common autoimmune bullous diseases seen in Hong Kong (comparison summarised in Table 3). The diagnosis of autoimmune skin diseases requires clinico-pathological correlation. Although newer ELISA kits are now available, they play a role in monitoring antibody titre but cannot completely replace DIF of biopsied skin in diagnosis of various autoimmune bullous diseases.

*Table 3. Comparison of clinical and histological findings among pemphigus foliaceus, pemphigus vulgaris and bullous pemphigoid*

| | Pemphigus foliaceus | Pemphigus vulgaris | Bullous pemphigoid |
|---|---|---|---|
| Lesion morphology | Erosions +/- crusting; intact blisters rarely seen | Erosions +/- crusting; intact blisters rarely seen | Intact blisters common; erosions seen only if blister ruptures |
| Distribution | Commonly found on seborrhoeic areas (face, upper trunk); no mucosal lesions seen | Mucosal erosions common as initial presentations, on progression both mucosal and cutaneous lesions develop | Flexural surfaces such as abdominal wall, groin or axilla, but can affect everywhere; mucosa may be involved in 10-40% of cases |
| Major histological findings | Subcorneal splitting, acantholysis | Suprabasal splitting, acantholysis | Subepidermal blisters, eosinophilic infiltration |
| Direct immunofluorescence | Intercellular IgG staining; C3 staining variably present | Intercellular IgG staining; C3 staining variably present | Linear basement membrane IgG + C3 staining |
| Correlation of antibody level (estimated by indirect immunofluorescence test) with disease activity | Present | Present | Absent |

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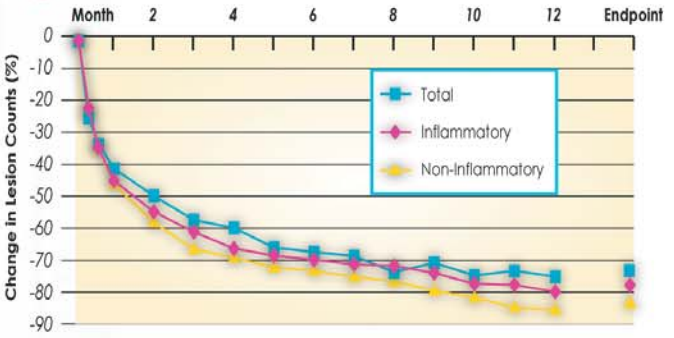


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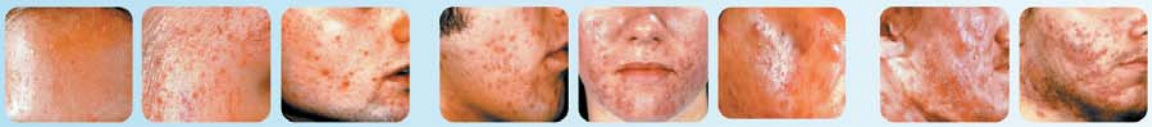

| Mild | | Moderate | | Severe |
|---|---|---|---|---|
| Comedonal | Papular/pustular | Papular/pustular | Nodular | Nodular/Congoblate |
| 1st choice: TOPICAL RETINOID | TOPICAL RETINOID + Topical Antimicrobial | TOPICAL RETINOID + Oral Antibiotic +/- BPO | TOPICAL RETINOID + Oral Antibiotic + BPO | Oral Isotretinoin |

*Differin targets the root cause and symptoms of acne* [2, 3]

*Differin prevents formation of microcomedones, the precursor lesions of inflammatory lesions and comedones.* [2]


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DIF-AD001-0808

# Diagnosis and Management of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

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## Introduction

Stevens-Johnson Syndrome(SJS) and Toxic Epidermal Necrolysis (TEN) are variants of a spectrum of conditions characterised by erythematous macules evolving to epidermal detachment and mucous membrane erosions. In SJS there is less than 10% body surface area involvement, in TEN more than 30% and 10-30% overlap cases.

It is important to be able to recognise Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) and manage them properly. The mortality rate of SJS and TEN is high: even in moderately severe cases it could be up to 30%. For those who survive, there could be troublesome late complications. Moreover, since the use of drug is the most important cause, the identification and removal of the causative medication is of paramount importance to halt the progression of the conditions and to prevent recurrence from inadvertent re-challenge.

## Recognising SJS and TEN

We could recognise SJS and TEN early if we are familiar with their clinical features, especially those earlier ones. Many patients with SJS and TEN begin with the prodromal symptoms of fever, headache and myalgia. The SJS and TEN skin eruptions1 first appear as erythematous then dusky or purpuric macules. The lesions are usually irregularly shaped, discrete in the beginning then coalesce with one another. Atypical target lesions could be seen but they are not the three-zone target lesions seen in erythema multiforme. The rash first appears on the face and upper part of the trunk and proximal part of the extremities and spread rapidly to the rest of the body. Lesions soon developed into flaccid blisters. For those non-blistered rash, Nikolsky sign (separation of epidermis from dermis with lateral pressure) can be demonstrated, which is an important though not pathognomonic sign. Finally the necrotic epidermis comes off leaving large areas of red exudative dermis exposed.

The mucous membrane is always involved in SJS and TEN, commonly precede the rash but sometimes after. Erythema is followed by painful erosions on the buccal, ocular and genital mucosae, and usually more then one site are involved. More than 80% of patients have conjunctival involvement, sometimes leads to corneal ulceration, anterior uveitis and synechiae. Ocular involvement in SJS and TEN could result in the most debilitating late complications.

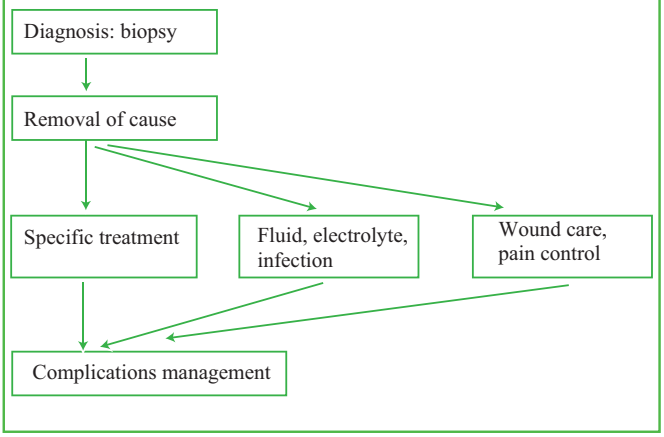
SJS and TEN do not limit themselves to the skin. Pulmonary and digestive system involvements are not uncommon. A quarter of patients have shortness of breath, hypoxia and haemoptysis, and the degree of pulmonary involvement is not necessary in proportion to the degree of skin involvement. Chest X-ray could show features of interstitial involvement but differentiation from infection is important, which could be helped with fibreoptic bronchoscopy. Gastrointestinal tract involvement will result in diarrhoea, malena and oesophageal necrosis. Renal involvement will result in proteinuria, haematuria and azotaemia.

The prodrome of fever, myalgia, headache; the appearance of dusky rash on the face and proximal limb; mucosal erosion, and the positive history of drug exposure should alert the physician to the possibility of SJS and TEN

## Managing Patients with SJS and TEN

SJS and TEN are life threatening conditions that need intensive care with experienced physicians and specialis nurses and multidisciplinary team work. The framework of the management is depicted in Chart 1.

*Chart 1 Management of SJS/TEN*




## Diagnosis

All suspected cases of SJS and TEN should be confirmed by skin biopsy for histologic and immunofluorescence examinations. Early lesion shows suprabasal layer apoptotic keratinocytes. Later lesion shows full-thickness epidermal necrosis and separation of epidermis from dermis. A number of important

conditions mimic SJS and TEN (Table 1) hence a histological evidence is important. Since 90% SJS and TEN has mucous membrane involvement the absence of such should prompt one to consider alternative diagnosis.

*Table 1 Mimickers of SJS and TEN*

| |
|---|
| Erythema multiforme major |
| Staphylococcal scalded skin syndrome |
| Purpura fulminant |
| Disseminated intravascular coagulation with skin necrosis |
| Acute generalised exanthematous pustulosis |
| Generalised bullous fixed drug eruption |
| Chemical toxicity (methotrexate, colchicines etc) |
| Burns |
| Graft-versus-host disease |
| Pemphigus |

Erythema multiforme (EM) could easily be mixed with SJS since both present with rash and oral mucosal erosion. The classification by Bastuji-Garin[2] separated erythema multiforme from SJS/TEN although it is not universally agreed. EM is different from SJS and TEN in many ways (Table 2). Infection is the major cause of EM and the commonest implicated infections are Herpes simplex and Mycoplasma pneumoniae although some other infectious agents have been reported, whereas drug is considered as an uncommon cause. The typical target lesions in EM have three concentric zones: central dusky disk, middle pale ring, outermost erythematous halo and they are not found in SJS and TEN. Characteristically all lesions of EM are papular and in acral distribution at least initially whereas in SJS and TEN rash start on face and proximal limbs. Although in EM there could also be mucosal involvement they are mostly limited to oral mucosa.

*Table 2 Comparing EM and SJS/TEN*

| EM | SJS/TEN |
|---|---|
| Infection: Herpes simplex, Mycoplasma pneumoniae | Drug causes |
| Papular erythematous lesions | Macular dusky lesions |
| Typical targets with three zones | Target lesions atypical |
| Aral distribution initially | Face and proximal limb initially |
| 70-% mucosal involvement but limited to oral mucosa usually | 90% mucosal involvement and many on more than one sites |
| Fever and constitutional symptoms absent | Fever, headache, myalgia common |
| Most <10% body surface area | Extensive with epidermal necrolysis |
| Mild course, recovers in 1-4 weeks | High mortality in severe cases |
| Recurrence common and many are herpes simplex related | Recurrence uncommon unless causative drugs re-challenged |

Staphylococcal scalded skin syndrome (SSSS) presents initially as a macular exanthema which might quickly evolve to blistering eruption with positive Nikolsky's sign and mimic SJS and TEN. SSSS more commonly occurs in infants or adults with renal failure. A Tzanck smear will find acantholytic cells in SSSS but not TEN. Skin biopsy with frozen section examination will find intradermal cleavage with acantholysis in the subgranular layer whereas in SJS and TEN full-thickness epidermal necrosis and dermal-epidermal separation are found. The diagnosis of SSSS instead of SJS/TEN will enable the early use of antibiotics against Staphylococcus.

## Removal of Cause

In 70% of SJS and TEN drug cause could be identified and more than 100 agents have been reported3. Drug history taken carefully and repeatedly, involving family members, enquiring family doctors, and taking over-the-counter non-prescription items into consideration are necessary before the causative agent can be identified. Since many patients could be taking several agents at the same time, the true causative agent could be hard to isolate. The temporal relationship between the intake of the agent and onset of condition is an important factor. SJS and TEN usually begins less than 8 weeks but more than 4 days from the first intake of the agent. Look for drugs that were added within this period. Only re-challenged drugs will elicit the condition in a few hours. Some medications have higher risk of causing SJS and TEN whereas in some other medications SJS and TEN has not been reported (Table 3). Infection is not a common cause of SJS and TEN although there have been case reports of Mycoplasma pneumonia. The identified culprit should be removed immediately and labelled "allergic" so that it would not be re-challenged inadvertently. In case of complicated drug history and a definite single causative agent could not be identified, only the necessary medications should be retained.

*Table 3 Drugs and SJS/TEN*

| High Risk | No reports of SJS/TEN |
|---|---|
| Allopurinol | Angiotensin-converting enzyme inhibitors |
| Carbamazepine | Aspirin |
| Lamotrigine | Aldactone |
| Nevirapine | Beta-blockers |
| NSAIDs(Oxicam) | Calcium channel inhibitors |
| Phenobarbital | Furosemide |
| Phenytoin | Sulfonylurea |
| Phenylbutazone | Thiazide diuretics |
| Sulphadiazine | |
| Sulfapyridine | |
| Sulfamethoxazole | |
| Sulfasalazine | |

## Specific Treatment

SJS and TEN are life threatening conditions. The success of treatment depends on early recognition of the condition, prompt removal of the causative medications and intensive supportive care in a well-equipped hospital.[4] Several agents with anti-inflammatory or immunosuppressive properties have been tried to alter the course of the disease but no single agent has their efficacy clearly proven by clinical trials.

**1. Intravenous Immunoglobulin (IVIG)**

Prepared from pooled plasma, IVIG contains immune antibodies that interfere with the apoptotic pathway mediated by the Fas ligand and receptor. Theoretically it is best to give IVIG early (within 24-72 hours from first appearance of bullae)[4,5] before Fas ligand and receptor binding has occurred, although it may still be effective if new bullae are still appearing. Sucrose-depleted IVIG is preferred since it has lower possibility of renal toxicity. Patient with IgA deficiency will develop anaphylaxis to IVIG. It is best to obtain a patient's IgA level before administering but awaiting the report might delay treatment. History of recurrent sinopulmonary infection and gastrointestinal infection may help to identify those with IgA deficiency which is very rare.

Results of studies of IVIG on SJS and TEN has been conflicting, and IVIG should not be considered as a routine treatment. Some studies have suggested the higher dose of 3g/kg total dose given over 3 days has better effects over the lower dose of 2g/kg total dose.

**2. Systemic Corticosteroid**
Some studies have advocated the use of systemic corticosteroids in the early stage of SJS and TEN. Other studies failed to prove the effect of the agent and have demonstrated an increase in the chance of sepsis and other complications. Balancing available evidence especially the more recent ones,[1] systemic corticosteroids cannot be recommended in TEN. Its use in SJS is still controversial but should not be recommended when extensive skin loss has already occurred.

**3. Cyclosporin A**
Supported by favourable outcomes[6] in several case reports and series, which used cyclosporin A at a dose of 3-4mg/kg/day in short term, thus avoiding its side effects which commonly occur in long term use, this agent seems promising but more comprehensive studies are needed.

**4. Other Agents**
Theoretically removal of the offending medication, its metabolites or cytokines by plasmapheresis or haemodialysis could help the improvement of SJS and TEN. However the lack of good clinical evidence and the risk of sepsis associated with in-dwelling catheter does not support these as recommendable treatments. Thalidomide[7] based on its anti-TNF effect has been tried but the study was prematurely terminated since excess mortality was reported.

## Management of Fluid, Electrolyte, Respiration and Infection

In the absence of proven effective specific agent, the success in treating SJS and TEN depends very much on supportive care. Since SJS and TEN can deteriorate rapidly, intensive care unit or burn centre care is recommended. Fluid loss and electrolyte imbalance should be closely monitored and corrected. Peripheral line is more recommendable than central, which has a higher chance of infection, but good peripheral venous access is difficult to find. All lines should be checked for signs of infection daily and changed two times a week with tips of lines and catheters sent for culture. Nutrition support with nasogastric tube helps healing. Respiratory rate and oxymeter monitoring are important. Raised urea level, blood glucose above 14mm/L and neutropenia are unfavourable prognostic factors and should be monitored.

Sepsis is the main cause of death. Cultures should be taken frequently from the cutaneous erosions, mucosal erosions, blood and urine to obtain the microbiology and their sensitivity profile. Signs of infection should be monitored closely and systemic antibiotics should be promptly administered when signs of infections (fever or falling body temperature, rigour, hypotension, decrease in urinary output, respiratory failure, poor glycaemic control and impaired consciousness, etc) are detected. Prophylactic antibiotic is contraindicated since this will encourage the appearance of resistant strains.

## Wound Care and Pain Control

Painstaking wound care is the backbone to management of SJS and TEN.[1,4] Good wound care reduces the chance of infection and pain. There is no standard protocol on the wound dressing. Various non-stick dressing has been used but sulfa-containing material should be avoided to prevent systemic sensitisation and leucopenia. Use air-fluidised mattresses to prevent pressure sore. The environment temperature is maintained at 28-30 degree Celsius to prevent hypothermia. Debridement of necrotic epidermis is not necessary. Adequate pain control many a time needs morphine group of analgesics. Respiratory depression should be watched out if opiates are used.

Oral mucosal ulceration is very painful. Chlorhexidine rinses help in maintaining good hygiene and white-soft paraffin on the lips relieves the pain. Complications on the eyes could result in blindness and an ophthalmologist's care is necessary. Artificial tears, antibiotics eye drops every two hourly and mechanical disruption of early synechiae is needed.

## Complications

Sepsis is the most important cause of mortality. Extensive erosions put patients at risk of infection by bacteria and fungi which will result in pulmonary complications and multi-organ failure. If respiratory failure develops, ventilation support is needed.

Late ophthalmic complications are seen in up to 75% of patients, hence early treatment is needed. Hyperpigmentation and hypopigmentation are common and sometimes scars and nail dystrophy may result. Genital adhesions resulting in dyspareunia, pain and bleeding should be watched out. Gastrointestinal, bronchial, urethral and anal complications are less common. Post-traumatic stress disorder is also possible and some patients may need psychiatrist's care. All patients recovering from SJS and TEN should be followed-up for development of these complications which could be delayed but debilitating.

## Prognosis

Depending on the severity, the clinical course of SJS and TEN may last up to a few weeks. It should be noted that the prognosis is not related to type or dose of the causative medication. A SCORTEN prognostic scoring system[8] has been developed to correlate mortality with selected parameters.

| Prognostic factors | Points | SCORTEN | Mortality Rate |
|---|---|---|---|
| ▪ Age > 40 | 1 | 0-1 | 3.2% |
| ▪ Heart rate >120/min | 1 | 2 | 12.1% |
| ▪ Cancer or haematologic malignancy | 1 | 3 | 35.8% |
| ▪ >10% body surface area | 1 | 4 | 58.3% |
| ▪ Serum urea >10mm/L | 1 | >5 | 90% |
| ▪ Serum bicarbonate<20mm/L | 1 | | |
| ▪ Serum glucose >14mm/L | 1 | | |

## Conclusion

Successful management of SJS and TEN requires the early recognition of the conditions, diagnosis with biopsy, identification and removal of the causative drugs and intensive multidisciplinary management in a hospital with experienced medical and nursing personnel.

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# Update on Applications of IVIg in Immunologically-related Dermatoses

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## Introduction

IVIg has been used as an immunomodulator in various specialties and represents a novel therapy for immune dysfunction. Its use for immune-mediated dermatoses has increased rapidly in the last decade (or past decades), permitting a corresponding reduction of the immunosuppressive therapy and subsequent decrease in immunosuppressive drug-related adverse events.

A single donation of whole blood (450ml) yields approximately 15ml of plasma proteins, of which only 2-3ml is γ-globulin.[1] Since the 1980s, IVIg has been produced by fractionation of pooled human plasma from 3,000 to 5,000 donors for each batch. Safety measures have been taken during the preparation regarding the source of plasma and standard of microbial inactivation procedures.[2] The preparation currently used in HA hospitals is Intragam® P (CSL Limited, Australia). The plasma source is from the Hong Kong Red Cross Blood Transfusion Service. It contains maltose 10% as the sugar base. Each vial of Intragam® P (50ml) contains nearly 3g of IgG. There may be 'lot to lot' variations in purity, antibody activity and content of immunomodulatory proteins leading to differences in response to IVIg. [3]

## Mechanisms of Immunomodulation

IVIg exerts several immunomodulating properties. The precise mode of action is still not clearly understood. IVIg seems to act on suppression of pathogenic antibody production, neutralisation of antibody and complement-mediated effects by anti-idiotypic antibodies, T-cell activation and Fas/Fas ligand interaction.[4] Furthermore, the functional blockade of antibody Fc receptors on leukocytes, the modulation of cytokine profiles and increased T cell suppressor activity are other postulated mechanisms of action of IVIg.[5]

## Dermatological Indications

The number of dermatological conditions having reported usefulness with IVIG is ever increasing.(**Table. 1**) The majority of IVIg applications are "off-label" use given the scarcity of randomised controlled trials for most dermatologic entities. The general consensus is that it should be considered as a second line therapy.[6] It is indicated when the conditions fail to respond and continue to progress despite the standard treatments or when there are significant side effects resulted from the conventional treatments or contraindications to the use of long-term immunosuppressive agents such as concomitant tuberculosis.[7]

Benefits of IVIg have been proven in dermatomyositis resistant or partially responsive to conventional therapy as shown in randomised controlled trials with clearing of the rash, improvement of muscle strength and successful tapering of corticosteroid.[8] Clinical and serologic improvements following IVIG were noted in different series of patients with systemic lupus erythematosus.[9] The treatment of scleroderma with immunosuppressive therapy is difficult and the disease often shows a progressive course. Significant improvements of scleroderma including regression of dystrophic calcification have been observed with the use of IVIg on a monthly basis in some case reports.[10,11] Kawasaki disease is one of the most well known indications to use IVIg in paediatric patients given within the first 10 days to prevent coronary anuerysms.[12] The current recommended dose for Kawasaki disease is a single dose of 2g/kg over 8 to 12 hours in combination with aspirin.

There are ample publications on the use of IVIg in autoimmune mucocutaneous blistering diseases but the majority reporting favourable responses are uncontrolled series and anecdotal reports.[13] The diseases include pemphigus vulgaris, pemphigus foliaceus, cicatricial pemphigoid, bullous pemphigoid, linear IgA disease and epidermolysis bullosa acquisita.[11,14,15] In general, this treatment appears to have greater efficacy as an adjunctive therapy than monotherapy.[16] Some authors advocate the concurrent use of immunosuppressive agents to improve the effectiveness of IVIg therapy by inhibiting antibody synthesis to offset the rebound in autoantibody level that follows its depletion by IVIg.[17] In a review of 21 patients with severe pemphigus, 81% showed clinical improvement and were able to reduce systemic immunosuppressants.[15,18]

Stevens-Johnson syndrome (SJS) / toxic epidermal necrolysis (TEN) is a life threatening mucocutaneous reactions to drug characterised by extensive damage of epidermis, leading to blistering and erosions. The mortality, ranging from 16-30%, is due to sepsis and multiorgan failure following the loss of epidermis. Apoptosis owing to the up-regulation of death receptor ligand (FasL) on keratinocytes is the potential mechanism causing massive keratinocyte death in TEN.[19] Naturally occurring anti-Fas antibodies in IVIg were found to be effective in inhibiting Fas-mediated keratinocyte apoptosis induced by FasL in vitro. In a

local series, six consecutive patients (TEN=4 and SJS=2) with mean body surface involvement 45% (range: 10-90%) received IVIg at 1g/kg daily for 3 days at a mean of 3.3 days after onset. No adverse effects of IVIg were observed. Interruption of further skin detachment occurred in 4.6 ± 0.9 days and complete wound healing took an average of 9.6± 2.1 days after IVIG started.[20] One patient died (mortality 16.7%). For the indication of SJS and TEN, it should be given as early as possible once the condition is diagnosed so as to achieve maximal effects.

Use of IVIg has been reported anecdotally in other dermatoses including systemic vasculitis, pyoderma gangrenosum, livedoid vasculopathy, drug hypersensitivity syndrome, nephrogenic fibrosing dermopathy, pretibial myxedema and scleromyxedema.[11,13,21-24] There is insufficient evidence to recommend its use in atopic dermatitis and chronic idiopathic urticaria because of the heterogeneous mechanisms underlying these diseases.[1] It remains a therapeutic option in patients with severe autoantibody-mediated chronic urticaria demonstrated by positive autologous interdermal serum test.[2]

## Safety

IVIg therapy is generally well tolerated and its side effects are mostly mild and self-limiting. The incidence of adverse events reported is less than 5%.[3] The safety profile of IVIg is more favourable than other immunosuppressive agents. The reported adverse effects include fever, chills, flushing, myalgia, nausea, headache, hypertension and hypotension.[25] **(Table.2)** Development of cutaneous side effects is not uncommon and pompholyx, palpable purpura and generalised eczematous eruptions have been noted several days after IVIg.[2,31] These are fortunately self-limiting and can be treated with topical steroid and emollients. Many of the acute side effects can be settled by slowing down or temporarily discontinuing the infusion. Intravenous hydrocortisone and antihistamine may be given if necessary.

Aseptic meningitis is occasionally observed and presents with headache, photophobia and nuchal rigidity. Haemolysis and neutropenia are potential haematological complications. There is a theoretical risk of infectious complications and patients should be warned of the remote risk of blood borne infections related to IVIg.[26] Anaphylaxis has been reported due to the presence of anti-IgA antibodies in selective IgA deficiency (SIgAD) patients. IVIg contains trace amount of IgA. However, IgA level determination may not be feasible in emergency situation. Fortunately, the prevalence of selective IgA deficiency in Chinese population was 0.0024%, contrasting to incidence of 1 in 700 in Western population and 25% of SIgAD patients develop anti-IgA antibodies in Japanese population.[27,28]

Caution must also be taken when IVIg is administered to patients with renal impairment owing to the toxic effects to renal tubules, especially when sucrose-based preparation is used. Acute renal failure has been reported after IVIg therapy, particularly in elderly patients with renal impairment and dehydration.[29] There are increasing number of reports of thrombotic complication after administering IVIg related to increase in blood viscosity.[30] The risk seems to be greater when higher doses or rapid infusion rates are adopted.

## Administration and Precautions

The optimum dose, duration and maintenance regime of IVIg have not been determined. The doses range from 1-3g/kg per cycle.[32] Infusion is usually given over 4 to 6 hours as in-patients. For most chronic dermatologic indications, the current evidence supports the dose of 2g/kg per cycle administered over 2 to 5 days. The half-life of IVIg is approximately 4 weeks. An average of 4 to 6 monthly cycles are used in most studies if maintenance treatment is required.

Live vaccination, such as MMR, should be avoided 2 weeks before and 3 months after the IVIg administration because of the interference of the development of immune response.[2] Baseline blood tests comprising complete blood count, liver and renal function tests should be checked. Measuring immunoglobulin levels is advised to screen for IgA deficiency especially in elective cases with pre-existing immunodeficiency. Rhematoid factors and cryoglobulins should be checked if there are pre-existing purpuric rashes and arthralgia. There is increased risks of acute renal failure after IVIg infusion resulted from immunoprecipitation in the presence of cryoglobulinaemia.[33] The risk is particularly high in patients with B-cell lymphoma associated with raised serum IgM levels.[34]

Depending on the risk of thromboembolism and fluid status of the patients, particularly with cardiac or renal failure, IVIg infusion should be slow and not exceed 4ml/min to reduce the risk of fluid overload. Adequate hydration is desirable to minimise the renal toxicity. Close monitoring of the vital signs and body temperature is important, as untoward reactions are often apparent during the first hour of administration. Vital signs should be monitored every 15 minutes for 1 hour and then hourly. Complete blood count and renal function tests should be monitored following IVIg infusion.

## Conclusion

Although the use of IVIg in treating dermatologic conditions seems promising, the effectiveness remains to be confirmed as the number of patients in most of the reported conditions is small. These largely uncontrolled and heterogeneous studies should be interpreted with caution in view of the likely reporting bias for favourable outcomes, differences in IVIg preparations, dosing schedules, severity of disease and prior use of immunosuppressive agents. Kawasaki disease, dermatomyositis and autoimmune blistering diseases have the greatest evidence for efficacy of IVIg. The perceived benefits of IVIg treatment should be balanced against the risk and the cost of therapy as opposed to the adverse effects of other systemic immunosuppressants. It should be considered on an individual basis, according to severity and relative contra-indication of other potential therapy.

It appears that IVIg is more useful as an adjuvant therapy or steroid sparing purposes, given the excellent overall tolerability. Despite some adverse events, the cost and inconvenience of hospital admission, IVIg represents a therapeutic option in patients with selected immune-mediated dermatoses.

*Table 1.*

| IVIg for dermatologic indications | |
|---|---|
| ***Autoimmune bullous dermatoses*** | ***Rhematological disorders*** |
| Pemphigus vulgaris and foliaceus | Dermatomyositis |
| Bullous pemphigoid | Scleroderma |
| Cicatricial pemphigoid | Systemic lupus erythematosus |
| Epidermolysis bullosa acquisita | ***Other dermatoses*** |
| Pemphigoid gestationis | Chronic idiopathic urticaria |
| Linear IgA bullous dermatosis | Graft-versus-host disease |
| ***Drug hypersensitivity*** | Pyoderma gangrenosum |
| Toxic epidermal necrolysis / Stevens-Johnson syndrome | Livedoid vasculopathy |
| Drug reaction with eosinophilia and systemic symptoms | Scleromyxedema<br>Nephrogenic fibrosing dermopathy |
| | Pretibial myxedema |

*Table 2*

| Adverse effects of IVIg therapy |
|---|
| Fever, chills, flu-like symptoms |
| Headache |
| Aseptic meningitis |
| Hypertension |
| Hypotension or shock |
| Transiently deranged liver or renal function tests |
| Urticarial eruption |
| Palpable purpura |
| Generalised eczema |
| Pompholyx |

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# 66th Annual Meeting of the American Academy of Dermatology, San Antonio, Texas. 1-5 February, 2008

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## Update in Paediatric Dermatology

## (I) Current Concepts in Atopic Dermatitis

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### Background

Atopic dermatitis is an inflammatory skin condition seen in patients with characteristic eczematous lesions clinically. The prevalence in children is 10-20% and in adults is about 2%. Atopy is a familial predisposition to develop hay fever, asthma and atopic dermatitis in association with high levels of serum IgE in most patients. Atopic dermatitis is likely to result from a combination of factors, including genetic susceptibility, environment, skin barrier defects, infections and immunologic factors. Importance of immune defect is illustrated by observation of atopic dermatitis being transferred during bone marrow transplantation.

### The Role of Th2 Cells

The immunoglobulin isotype class switching to production of IgE is induced by IL-4 and IL-13 which are Th2 cytokines, implicating Th2 cells in the pathogenesis of atopy and atopic dermatitis. Increased numbers of activated CLA+ CD4 T cells are found in acute lesions of atopic dermatitis, with elevated levels of Th2 (IL-4, IL-5, IL-13) and decreased Th1 (IFN-γ ) cytokines. Decreased CCR6-expressing (Th1-associated chemokine receptor) and increased CCR4-expressing (Th2-associated) T cells are found in lesions of atopic dermatitis. There was one report of increased IL-17 in acute skin lesions of atopic dermatitis compared with chronic lesions or uninvolved skin, but the role for Th-17 cells is not clear.

### Other Iimmunologic Abnormalities in Atopic Dermatitis

There is increased expression of Fc£`R1 on dendritic cells in skin and monocytes in blood. There is increased expression of cAMP-phosphodiesterase, increased PGE2 and increased IL-10 production by monocytes. There are B cells expressed high levels of CD86 (costimulatory molecule) and there are high levels of TSLP (thymic stromal lymphopoietin) in keratinocytes. TSLP activates dendritic cells to prime naive CD4 T cells to produce Th2 cytokines.

### Genetics of Atopic Dermatitis: More Recent Findings

1. 1. Toll-like receptor 2 (TLR2) is one member of a family of innate immune system receptors referred to as the "toll-like receptors". They are involved in recognition of conserved molecular patterns on microbes and aid in alerting the immune system to invading pathogens. Missense mutation in *TLR2* gene was found with increased frequency in atopic dermatitis which correlated with greater severity of atopic dermatitis, higher IgE and greater susceptibility to *Staphylococcus aureus*.

2. Filaggrin is an integral component of the keratin cytoskeleton and is critical for epidermal barrier function. The gene is localised to chromosome 1q21. Two common loss-of-function mutations in the gene encoding filaggrin were recently found to be associated with an increased risk of moderate-severe atopic dermatitis, as well as asthma that was associated with atopic dermatitis.

### The Relationship Between Allergen Specific IgE Responses and the Skin Lesions of Atopic Dermatitis

The severity of atopic dermatitis and early onset in infancy correlate with serum IgE levels. Both are risk factors for development of upper airway disease. It is proposed that IgE on the surface of Langerhans cells in the skin can act to focus antigen presentation and facilitate T cell activation; this would explain how exposure to specific allergens might trigger flares of atopic dermatitis.

Recent well-controlled studies argue against a role for dust mites in the flare of atopic dermatitis, while food triggers may play a role in a small percentage of patients with flares of skin disease. It is believed that autoantigens may play a role especially in chronic skin lesions and IgE autoantibodies directed against human skin proteins have been described.

### The Role of Staphylococcus Aureus

There is increased colonisation of skin lesions in atopic dermatitis with *Staphylococcus aureus* (*S. aureus*) and an antibiotic is useful in treatment. The release of superantigens and α-toxin by *S. aureus exacerbates* inflammation. α-toxin can also induce release of

TNF-α, arachidonic acid and platelet-activating factor. In atopic dermatitis, the skin lesion shows increased expression of *S. aureus* adhesins and these are induced by IL-4.

### The Rising Incidence of Aatopic Disease: Does the Hygiene Hypothesis Explain it All?

The incidence of all atopic diseases doubled over the past 2-3 decades and the rate of rise suggested environmental influence. "Hygiene Hypothesis" postulated that increased atopic disease is a result of decreased exposure to infections in early life; based on a study(or studies) showing increased number of siblings is protective for development of allergies. Further studies have supported the observation that early attendance at daycare (another surrogate marker for infectious exposure) is also protective for development of atopy. The original theory put forth was that exposure to infections stimulated Th1 immune responses, thereby suppresses Th2 responses which are responsible for atopic dermatitis; i.e., without the Th1 inducing infections, Th2 responses were left unopposed.

More recently, it has been proposed that a failure to develop "regulatory T cells" may account for increases in both allergic and autoimmune diseases. Regulatory T cells develop as part of the natural response to infections, helping to contain the pathogen-directed inflammatory response. These cells are then capable of suppressing both unwanted Th1 and Th2 type immune responses.

Interestingly, patients with IPEX syndrome (immune dysregulation, polyendocrinopathy, enteropathy and X-linked inheritance) have a mutation in FOXP3. This gene has been shown to be critical for development of CD25+ T regulatory cells. These patients display both autoimmune disease and eczema.

## (II) Kawasaki Disease

### *Emergency Paediatric Dermatology*

Speaker: Norman Levine, MD, FAAD; Tucson, Arizona

### *Paediatric Diagnostic Update*

Speaker: Robert Sidbury, MD; Dermatology Program, Department of Paediatrics, Division of Immunology, Children's Hospital Boston, Harvard Medical School

Kawasaki disease is one of the leading causes of paediatric acquired heart disease. It is also a potential risk for adult ischaemic heart disease and sudden death in young adults. It occurs most commonly in Asians and Japanese. The cause is unknown but multiple theories were suggested including adenovirus infection, novel human coronavirus infection and environmental pollens.

The pathogenesis involves inflammation of the arteries with proteinases and cytokines release. There is a possible role of IgA secreting plasma cells related to respiratory viral infection. Coronary artery lesions developed and resulted in aneurysmal dilatation and later stenosis. There is premature atherosclerosis.

The classical clinical diagnostic criteria are fever for more than five days. In addition there are cervical lymphadenopathy (only 15% in US), non-exudative conjunctivitis (87%), crusted lip and strawberry tongue (90%), truncal exanthem (85%), and palmoplantar erythema and desquamation (90%).[1] The diagnosis is unusual in patients with age more than 10 years. However it can also be seen in adults with similar clinical features. Adult patients have more hepatitis (65% vs. 10%) and arthralgia (61% vs. 25%) than children, but there are less coronary aneurysms (5% vs. 20%) and thrombocytosis (55% vs. 100%) in adults than children. If the clinical features are incomplete, there are some dermatologic findings useful for diagnosis, such as bilateral groin desquamation in acute phase (days 1-4) and fingertip desquamation in subacute phase (days 8-12). There may be micropustular eruption, reactivation of BCG and flare of psoriasis.

Laboratory findings include elevated ESR, CRP and leucocytes. There may be echocardiographic findings of coronary aneurysm.

The principal management is IVIg and aspirin. IVIg is given in dose of 1-2g/kg body weight in single infusion. Repeat of therapy is necessary if there is evidence of persistent inflammation. High dose aspirin (50-100mg/kg body weight) must be given within 10 days of fever onset for best effect.

Recent studies have mixed results regarding the use of systemic corticosteroid as adjunct to IVIg therapy in Kawasaki disease. The addition of steroid to IVIg compared with IVIg alone improves outcome in one study with decreased number of aneurysms, shorter duration of fever, faster normalisation of laboratory results and fewer initial treatment failures.[2] In another study, however, there is no difference in outcomes between the patients with or without corticosteroid as adjunctive therapy.[3]

About 10-15% patients with Kawasaki disease fail initial therapy of IVIg infusion alone and 3-4% fail second dose of IVIg. These non-responders have refractory Kawasaki disease and they usually have similar baseline characteristics with the responders. These patients have higher risks of coronary artery aneurysm and later complications. Second line treatment for refractory disease such as cyclophosphamide, plasma exchange, cyclosporine and infliximab have been reported but not yet supported by randomised trials.

### References

1. Newburger JW et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. Circulation 2004; 110: 2747-71.
2. Newburger JW et al. Randomized trial of corticosteroid therapy for primary treatment of Kawasaki disease. NEJM 2007; 356: 663-75.
3. Inoue Y et al. A multicenter prospective randomized trial of corticosteroids in primary therapy for Kawasaki disease: clinical course and coronary artery outcome. J Pediatr 2006; 149: 336-41.

# Let's Go Together - Enjoy the Nature of Hong Kong

Dr. CK Kwan

**Dr. CK Kwan**

MBBS(HK), MRCP (UK)

*Yaumatei Dermatology Clinic, Social Hygiene Service*

As time flies, we will step into November soon. Everyone knows that Autumn has come. It is a nice and the most suitable atmosphere in Hong Kong for outdoor activities. The weather is good with beautiful sun-shine and the temperature is comfortable that is not too hot or too cold. Therefore, it is a peak season for hiking and the famous hiking event - Trail Walker is also held in November every year. It is the characteristic of Hong Kong that no one has to travel a long time to go to the countryside. Around 40% of Hong Kong area is covered by the country park. As the citizen in this cosmopolitan city, everyone can easily enjoy hiking in the arms of her nature.

Hong Kong is far more than a modern city. She boasts some wonderful countryside, with hills, forests, old villages, waterfalls, and islands. There are many trails that range from gentle strolls to tough hikes. There are four main trails - Hong Kong Trail, MacLehose Trail, Wilson Trail and Lantau Trail. They can take you to visit different parts of Hong Kong. Hong Kong Trail joins the western part to the eastern part of Hong Kong Island. It brings you from the Peak (山頂) to Big Wave Bay (大浪灣) with total 50 kilometres. MacLehose Trail is a famous trail across the east to the west of New Territories. The 100 km long pathway takes you from Sai Kung (西貢) to Kowloon peninsula then Shing Mun Reservoir (城門水塘) and finally to Tuen Mun (屯門). Wilson Trail is similar to MacLehose Trail that brings you to visit the most southern part of Hong Kong Island - Stanley (赤柱) to the most northern part of New Territories - Nan Chung (南涌) which is quite near to the boundary of Hong Kong. The total length is 78 km. Lantau Trail is the main hiking track on Lantau Island. It is a 70 km large circle situated at the south part of Lantau Island. It starts at Mui Wo (梅窩) then goes through the third highest mountain - Tai Tung Shan (大東山) and the second highest mountain - Lantau Peak (鳳凰山) of Hong Kong. It also visits the old fishing village - Tai O (大澳) and joins the Shek Pik reservoir (石壁水塘) to the Chi Ma Wan Peninsula (芝麻灣半島). It ends at Mui Wo again. I would grasp this opportunity to introduce some of the hiking paths so that we can enjoy the fun in hiking and the silence in her of nature.

## Hong Kong Island - Shek O Road (石澳道) to Big Wave Bay(大浪灣)

This path is located at the Shek O Country Park. It starts from To Tei Wan (土地灣) and ends at Big Wave Bay(大浪灣). After an around 45 minutes climbing upward, we reach the Dragon's Back (龍脊). It is the ridgetop between Wan Cham Shan (雲枕山) and Shek O Peak (打爛埕頂山). As it looks like the spine of a dragon, so it is named. It shows the full natural beauty of east coast of Hong Kong. The stunning view includes Waglan Island (橫瀾島) and Tung Lung Island (東龍島). Most people will follow the sign of Hong Kong Trail at the end to enter a jungle and then down to Big Wave Village (大浪灣村) . However, I suggest you to continue walking along the watercatch till the next exit to Big Wave Beach (大浪灣海灘). The scene of second exit is more beauty. We can see the endless sea and how the sky and sea are joined together at the infinity end.

## Sai Kung Peninsula - Long Ke Wan (浪茄灣) to Pak Tam Au(北潭坳)

This path lies in Sai Kung East Country Park. It is suitable for experienced walkers as it needs to climb up and down for several hills. The most attractive thing is the stunning mountain and sea scenery. It starts at Long Ke Wan (浪茄灣) and then climbs up Sai Wan Shan (西灣山). It is not easy even though the hill is not so high. When we reach Chui Tung Au (吹筒坳) after passing through the Sai Wan Shan, we meet the sea breeze and four beautiful and peaceful beaches lying in front of our eyes. They are Tai Long Wan(s) (大浪灣) - Sai Wan (西灣), Ham Tin Wan (鹹田灣), Tai Wan (大灣) and Tung Wan (東灣). Down the path, we reach the Sai Wan Village (西灣村). It is an old and remote village. The seascape and coastal scenery between Sai Wan and Ham Tin Wan is delightful. However, after it, there is a long steep slope climbing up to the Tai Long Au (大浪坳) and it is a real challenge for the hikers. Beyond this challenge, we meet at Chek Keng (赤徑). It is an inshore village formed by rocky beach and mangroves coast. Mudskippers and fiddler crabs are often seen at low tide.

## Lantau Island - Ngong Ping (昂坪) to Lantau Peak (鳳凰山)

I love hiking on Lantau Island. In those days while I was working in Lantau few years ago, I often hiked in Lantau everywhere after finishing the work at weekends. Ngong Ping (昂坪) is a plateau situated between the Lantau Peak (鳳凰山) and Nei Lak Shan (彌勒山). Nowadays, everyone knows that the Great Buddha Statue is at Po Lin Monastery (寶蓮寺). Thousands of tourists go to visit the Great Buddha by bus or cable car (Ngong Ping 360). Before that, Ngong Ping was a very famous Tea Garden in Hong Kong. Many tea trees were planted. Unfortunately, these tea gardens are abandoned and are

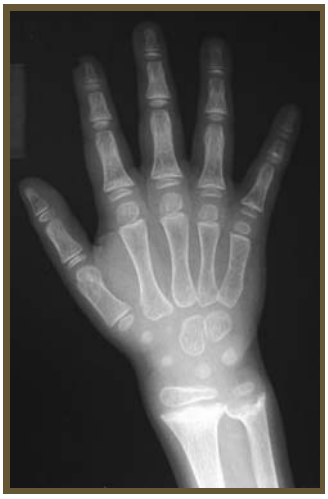
now overgrown by weeds. At Ngong Ping, there are lots of hiking paths. We can go along the north pathway to Shek Mun Kap (石門甲) and then Tung Chung (東涌). The characteristic of this track is passing through different monasteries and temples and is quite easy to walk. Also, we can go south down to Shek Pik Reservoir (石壁水塘) or go west to Keung Shan Road and then passing Keung Shan (羌山) to Tai O (大澳) which is the Venice of Hong Kong.

When we go to the west, we prepare to climb up the second highest mountain in Hong Kong - Lantau Peak (鳳凰山). This is definitely the main dish and is the representative of the Lantau Trail. It is quite hard to climb up to the top from Ngong Ping (昂坪) as the slope is steeper than the other side from Pak Kung Au (伯公坳). There is a place called "sky ladder"(天梯). It is named as the slope is very steep and like a ladder going to sky or heaven. In the old days, it is very dangerous as both sides are cliffs. Nowadays, the government sets up some metal hand-rails to make the path safer for the hikers. At the mountain top, we can have the unlimited scenery with the endless sea. Traditionally, Lantau Peak is the famous place to see the sun-rise.

The above hiking pathways are worthy to go, however, they are not easy and need experience. It is better to go with experienced hikers and with some training before. Actually, there are still lots of hiking paths that are suitable for the whole family including children and the elderly. Many books have this kind of information including the maps, transportations, difficulties and description of key scenery. Let's get started. May be, we will meet somewhere.

# Clinical Quiz

**Dr. Alice Wu**
*Associate Consultant, Queen Mary Hospital.*



## History:

M / 10yr. XR Left hand taken for bone age measurement.

## Questions:

1. What is your provisional diagnosis or differential diagnosis?
2. What investigations will you perform?
3. What is the commonest causative organism of your provisional diagnosis?
4. What is the treatment?

*(See P. 33 for answers)*

# FMSHK President Cup Soccer Five Tournament 2008

The FMSHK President Cup Soccer Five Tournament 2008 will be held from 12 October 2008 to 30 November 2008 at Ying Wa College. This year, there are 20 teams from a variety of medical societies, dental society and pharmaceutical companies competing for the President Cup.

The kick-off ceremony has been scheduled on 12 October 2008 at 1pm at Ying Wa College. Everyone is welcome to join the ceremony and watches (refer fixture) to share the fun of the games and to cheer the teams.


**The Soccer Five 2008 Committee Members and Team Captains**

# FMSHK President Cup Soccer Five Tournament 2008 Fixture

The tournament includes 17 teams, divided into four groups A, B, C, D.
Each section consists of 5 teams and a round robin format will be adopted
There will be a total of 72 matches competed in 4 days

| Date | Play (Team vs Team) | Schedule Time | Team Codes and Names | Participating Teams |
|---|---|---|---|---|
| | | | Opening Ceremony on 12/10/2008 1 pm - 3 pm<br>ALL team captains will be invited to attend | All Teams |
| 12/10/2008 | B1-B3 | 14:00-14:35 | | A1 B1 |
| Pitch 1 | B2-B4 | 14:35-15:10 | A1 Hong Kong Ophthalmological Society | A2 B2 |
| | B5-B3 | 15:10-15:45 | | A3 B3 |
| | B1-B4 | 15:45-16:20 | A2 Hong Kong Medical Association (Team 1) | A4 B4 |
| | B2-B5 | 16:20-16:55 | | A5 B5 |
| | A1-A2 | 16:55-17:30 | A3 Hong Kong Occupational Therapy Association | |
| | A3-A4 | 17:30-18:05 | | |
| | A5-A1 | 18:05-18:40 | A4 Hong Kong Dental Association (Student) | |
| | A2-A3 | 18:40-19:15 | | |
| | A4-A5 | 19:15-19:50 | A5 HKUSU Medical Society (Team 1) | |
| | | | B1 Hong Kong Dental Association | |
| Pitch 2 | C1-C2 | 14:00-14:35 | | C1 D1 |
| | C3-C4 | 14:35-15:10 | B2 Hong Kong Medical Association (Team 2) | C2 D2 |
| | C5-C1 | 15:10-15:45 | | C3 D3 |
| | C2-C3 | 15:45-16:20 | B3 HKUSU Medical Society (Team 2) | C4 D4 |
| | C4-C5 | 16:20-16:55 | | C5 D5 |
| | D1-D3 | 16:55-17:30 | B4 CUHK Medical Society | |
| | D2-D4 | 17:30-18:05 | | |
| | D5-D3 | 18:05-18:40 | B5 | |
| | D1-D4 | 18:40-19:15 | | |
| | D2-D5 | 19:15-19:50 | | |
| 19/10/2008 | B3-B4 | 14:00-14:35 | C1 Pfizer Corp HK (Team 1) | A1 B1 |
| | B1-B2 | 14:35-15:10 | | A2 B2 |
| Pitch 1 | B4-B5 | 15:10-15:45 | C2 Sanofi Aventis | A3 B3 |
| | B2-B3 | 15:45-16:20 | | A4 B4 |
| | B5-B1 | 16:20-16:55 | C3 Janssen Pharmaceutica | A5 B5 |
| | A1-A3 | 16:55-17:30 | | |
| | A2-A4 | 17:30-18:05 | C4 Zuellig Pharma Limited | |
| | A5-A3 | 18:05-18:40 | | |
| | A1-A4 | 18:40-19:15 | C5 | |
| | A2-A5 | 19:15-19:50 | | |
| | | | D1 Pfizer Corp HK (Team 2) | |
| Pitch 2 | D1-D2 | 14:00-14:35 | D2 AstraZeneca Hong Kong Limited | C1 D1 |
| | D3-D4 | 14:35-15:10 | | C2 D2 |
| | D5-D1 | 15:10-15:45 | D3 Jacobson Medical (Hong Kong) Ltd | C3 D3 |
| | D2-D3 | 15:45-16:20 | | C4 D4 |
| | D4-D5 | 16:20-16:55 | D4 IDS (Hong Kong) Limited | C5 D5 |
| | C1-C3 | 16:55-17:30 | | |
| | C2-C4 | 17:30-18:05 | D5 | |
| | C5-C3 | 18:05-18:40 | | |
| | C1-C4 | 18:40-19:15 | | |
| | C2-C5 | 19:15-19:50 | | |
| After 2 days of qualifying round robin, each team will have the teams' position within the group<br>The first two teams in each group will enter the final round robin. The 3, 4, 5th teams in each group will enter the knock-out round | | | | |
| 26/10/2008 | A1-B2 | 14:00-14:35 | The number here represents the position of the team after the first two days of round robin<br>e.g. A1 is the team with 1st position among Group A | |
| | C1-D2 | 14:35-15:10 | | |
| Knock-out Match | A5-B5 | 15:10-15:45 | | |
| | C5-D5 | 15:45-16:20 | | |
| | A1-D2 | 16:20-16:55 | | |
| Pitch 1 | B2-C1 | 16:55-17:30 | | |
| | LA5/B5-LC5/D5 | 17:30-18:05 | LA5/B5=loser of A5-B5(match3), LC5/D5=loser of C5-D5(match4) | positions 19&20 |
| | WA5/B5-WC5/D5 | 18:05-18:40 | WA5/B5=winner of A5-B5(match3), WC5/D5=winner of C5-D5(match4) | positions 17&18 |
| | A1-C1 | 18:40-19:15 | | |
| | B2-D2 | 19:15-19:50 | | |
| Pitch 2 | A2-B1 | 14:00-14:35 | | |
| | C2-D1 | 14:35-15:10 | | |
| | A4-B4 | 15:10-15:45 | | |
| | C4-D4 | 15:45-16:20 | | |
| | A2-D1 | 16:20-16:55 | | |
| | B1-C2 | 16:55-17:30 | | |
| | LA4/B4-LC4/D4 | 17:30-18:05 | LA4/B4=loser of A4-B4(match3), LC4/D4=loser of C4-D4(match4) | positions 15&16 |
| | WA4/B4-WC4/D4 | 18:05-18:40 | WA4/B4=winner of A4-B4(match3), WC4/D4=winner of C4-D4(match4) | positions 13&14 |
| | A2-C2 | 18:40-19:15 | | |
| | B1-D1 | 19:15-19:50 | | |
| After Day 3, we will have the teams' position in final session FA & FB<br>3rd & 4th teams will enter the knock-out<br>1st & 2nd teams will enter the final knock-out | | | | |
| 30/11/2008 | A3-B3 | 14:00-14:35 | | |
| | C3-D3 | 14:35-15:10 | | |
| Final Knock-out Match & Prize Presentation Ceremony<br>冠亞季軍賽 | FA3-FB4 | 15:10-15:45 | | |
| | FA4-FB3 | 15:45-16:20 | | |
| | FA1-FB2 | 16:20-16:55 | | |
| | FA2-FB1 | 16:55-17:30 | | |
| | LA3/B3-LC3/D3 | 17:30-18:05 | | positions 11&12 |
| | WA3/B3-WC3/D3 | 18:05-18:40 | | positons 9&10 |
| | LFA3/FB4-LFA4/FB3 | 18:40-19:15 | | positions 7&8 |
| | WFA3/FB4-WFA4/FB3 | 19:15-19:50 | | positions 5&6 |
| | LFA1/FB2-LFA2/FB1 | 19:50-20:25 | | positions 3&4 |
| | WFA1/FB2-WFA2/FB1 | 20:25-21:00 | | positions 1&2 |

Co-Chairmen: Mr. Nelson Lam, Dr. Kingsley Chan and Dr Liu Wing Hong
Secretariat: The Federation of Medical Societies of Hong Kong
Contact: Ms. Karen Chu, Executive Assistant, Tel: 2821 3515
Fixture Planned by Dr. Liu Wing Hong

10-Sep-08

## The New FMSHK Team (Administrative Assistant - Ms. Erica Hung)

Ms. Erica Hung has joined FMSHK as the Administrative Assistant since September 2008. Erica is equipped with professional secretary training and has over 10 years' experience serving the senior management of sizeable company. She is experienced in administrative work, event coordination and executive support and looks forward to offering her attributes to best serve the Federation.

# Society News

## News from Member Societies:

**The Hong Kong Society of Haematology**
Updated office-bearers for the year 2008-2009 are as follows: Chairman: Dr. Wing-yan AU; Honorary Secretary: Dr. Jason SO; Honorary Treasurer: Dr. Albert LIE

**Hong Kong College of Health Service Executives**
Updated office-bearers for the year 2008-2009 are as follows: President: Dr. Man-yung CHENG; Vice-President: Mr. Benjamin LEE; Honorary Secretary: Mr. Anders Chi-man YUEN; Honorary Treasurer: Dr. Shao-haei LIU

**The Hong Kong Medical Association**
Updated office-bearers for the year 2008-2009 are as follows: President: Dr. Hung-hing TSE; Vice-Presidents: Dr. Alvin Yee-shing CHAN, Dr. Pak-chin CHOW; Honorary Secretary: Dr. Chi-chiu LEUNG; Honorary Treasurer: Dr. Ernie Chi-fung LO

**The FMSHK would like to send its congratulations to the new office-bearers and looks forward to working together with their societies.**

## Society's Message

### The Hong Kong College of Health Service Executives

The Hong Kong College of Health Service Executives (HKCHSE), previously known as the HK Society of Health Service Executives, was inaugurated on May 20th 2005. The College is established in recognition of the emergence of health service management as a specialty in its own right and to promote for the professional advancement of health service managers. Our Mission is "To achieve excellence in health care service in Hong Kong through the advancement of professional and ethical standards in health service management".

During past years, we have organised lectures, workshops, conferences and seminars on management with themes ranging from management planning to health informatics to health economics. Local and overseas experts were invited to be our speakers, giving an interesting blend of international perspective from Mainland China, Singapore, Australia, United States and United Kingdom. Overseas Study Tours were organised for College Members each year. In 2006, a study tour was made to explore the Medical Tourism of Thailand while another Taiwan Study Tour was launched in 2007 for an in-depth visit on the National Health Insurance system there.

We have also entered into an affiliation agreement with the Australian College of Health Service Executives (ACHSE) for joint membership. By subscription to the Australian College through the HKCHSE, one will enjoy a discount rate on the annual subscription fee of the Australian College. This joint membership will enable our members to enjoy the benefit of both organisations at the same time. We shall also help our eligible members to take part in the Fellowship Examination organised by both Colleges jointly. Please visit our website http://www.hkchse.org and find out more.

| Sunday | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday |
|---|---|---|---|---|---|---|
| | | | 1 | ★ HKMA Council Meeting<br>2 | 3 | 4 |
| ★ HKMA Trailwalker Training Session VII (Stage 6 - 10)<br>★ HKMA CME Programme - Oncology & Haematology: Answers to the Questions in Your Mind<br>★ HKMA Structured CME Programme at Queen Elizabeth Hospital Year 08/09 (VII) - Neurosurgery and Pathology<br>★ HKMA Tennis Tournament<br>5 | ★ FMSHK Officers' Meeting<br>6 | 7 | ★ Hong Kong Neurosurgical Society Monthly Academic Meeting - Special Lecture: Fundamentals of Electroencephalography (EEG)<br>8 | ★ Certificate Course on General Ophthalmology<br>★ HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2008 (X)<br>9 | 10 | ★ Refresher Course for Health Care Providers 2008/2009 - Update in ENT<br>★ Annual Scientific Meeting 2008 - Evidence-based Pain Management<br>11 |
| ★ HKMA Tennis Tournament<br>★ Annual Scientific Meeting 2008 - Evidence-based Pain Management<br>12 | 13 | ★ Certificate Course on Respiratory Medicine 2008<br>★ Certificate Course on Ward Management Module I Understanding Management Issues in the Workplace (Code No. TC-WM-0801)<br>14 | 15 | ★ FMSHK Executive Committee Meeting<br>★ Final Briefing Session of HKMA Trailwalker 2008<br>★ Certificate Course on General Ophthalmology<br>16 | ★ 7th Annual Scientific Symposium on Towards Total Health<br>17 | ★ 7th Annual Scientific Symposium on Towards Total Health<br>18 |
| ★ HKMA Tennis Tournament<br>★ HKMA Trailwalker Training Session VIII (Stage 1 - 5)<br>★ HKMA Swimming Gala<br>19 | 20 | ★ Certificate Course on Respiratory Medicine 2008<br>★ Certificate Course on Ward Management Module I Understanding Management Issues in the Workplace (Code No. TC-WM-0801)<br>21 | ★ Clinical Updates 2008<br>22 | ★ Certificate Course on General Ophthalmology<br>23 | 24 | 25 |
| ★ HKMA Tennis Tournament<br>26 | 27 | ★ Certificate Course on Respiratory Medicine 2008<br>★ Certificate Course on Ward Management Module I Understanding Management Issues in the Workplace (Code No. TC-WM-0801)<br>28 | 29 | ★ Certificate Course on General Ophthalmology<br>★ HKMA Tin Shui Wai North/ Yuen Long Community Network Certificate Course<br>30 | 31 | |

| Date / Time | Function | Enquiry / Remarks |
|---|---|---|
| **2 THU** | **HKMA Council Meeting**<br>Organised by: The Hong Kong Medical Association Chariman: Dr. H.H. TSE # HKMA Head Office, 5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong | Ms. Christine WONG<br>Tel: 2527 8285 |
| **5 SUN** 7:00 am | **HKMA Trailwalker Training Session VII (Stage 6 - 10)**<br>Organised by: The Hong Kong Medical Association | Ms. Dora HO<br>Tel: 2527 8285 |
| 9:30 am | **HKMA CME Programme - Oncology & Haematology: Answers to the Questions in Your Mind**<br>Organised by: The Hong Kong Medical Association Speaker: Various # Shanghai Room, Level 8, Langham Hotel, Mongkok, Kowloon | Miss Viviane LAM<br>Tel: 2527 8452<br>2.5 CME Points |
| 2:00 pm | **HKMA Structured CME Programme at Queen Elizabeth Hospital Year 08/09 (VII) - Neurosurgery and Pathology**<br>Organised by: The Hong Kong Medical Association & Queen Elizabeth Hospital Speaker: Dr. KWOK Ngai Fung, Dr. WONG Yuk Wing & Dr. PONG Wai Mei # Lecture Theatre, G/F., Block D, Queen Elizabeth Hospital, Kowloon | Miss Viviane LAM<br>Tel: 2527 8452<br>(Registration fee is required)<br>3 CME Points |
| 7:30 pm *(12,19,26)* | **HKMA Tennis Tournament**<br>Organised by: The Hong Kong Medical Association # Kowloon Tong Club | Ms. Dora HO<br>Tel: 2527 8285 |
| **6 MON** 8:00 pm - 10:00pm | **FMSHK Officers' Meeting**<br>Organised by: The Federation of Medical Societies of Hong Kong # Gallop, 2/F., Hong Kong Jockey Club Club House, Shan Kwong Road, Happy Valley, Hong Kong | Ms. Paulina TANG<br>Tel: 2527 8898 Fax: 2865 0345 |
| **8 WED** 7:30 am | **Hong Kong Neurosurgical Society Monthly Academic Meeting - Special Lecture: Fundamentals of Electroencephalography (EEG)**<br>Organised by: Hong Kong Neurosurgical Society Speaker: Dr. FONG Ka Yeung # Seminar Room, G/F., Block A, Queen Elizabeth Hospital, Kowloon | Dr. Y.C. PO<br>Tel: 2990 3788 Fax: 2990 3789<br>2 CME Points |
| **9 THU** *(16,23,30)* | **Certificate Course on General Ophthalmology**<br>Organised by: The Federation of Medical Societies of Hong Kong & Hong Kong Society of Ophthalmology Speaker: Various # 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong | Ms. Erica HUNG<br>Tel: 2527 8898 Fax: 2865 0345 |
| 2:00 pm | **HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2008 (X)**<br>Organised by: The Hong Kong Medical Association and Hong Kong Sanatorium & Hospital Speaker: Dr. TANG Oi Shan # HKMA Dr. Li Shu Pui Professional Education Centre, 2/F., Chinese Club Building, 21-22 Connaught Road Cental, Hong Kong | Miss Viviane LAM<br>Tel: 2527 8452<br>(Registration fee is required)<br>1 CME Point |
| **11 SAT** 2:30 pm | **Refresher Course for Health Care Providers 2008/2009 - Update in ENT**<br>Organised by: The Hong Kong Medical Association & Our Lady of Maryknoll Hospital Speaker: Dr. LAU Sai Kit # Training Room II, 1/F., OPD Block, Our Lady of Maryknoll Hospital, 118 Shatin Pass Road, Wong Tai Sin, Kowloon | Ms. Clara TSANG<br>Tel: 2354 2440<br>2 CME Points |
| *(12)* | **Annual Scientific Meeting 2008 - Evidence-based Pain Management**<br>Organised by: Hong Kong Pain Society # Queen Elizabeth Hospital and Eaton Hotel Hong Kong | Secretariat<br>Tel: 2155 8557 / 2559 5888<br>Fax: 2559 6910<br>Email: meeting.hk@asia.cmpmedica.com |
| **14 TUE** *(21,28)* | **Certificate Course on Respiratory Medicine 2008**<br>Organised by: The Federation of Medical Societies of Hong Kong and Hong Kong Thoracic Society & American College of Chest Physicians (HK and Macau Chapter) Speaker: Various # 1/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong | Ms. Erica HUNG<br>Tel: 2527 8898 Fax: 2865 0345<br>9 CNE Points (6 sessions) |
| 6:30 pm - 9:30 pm *(21,28)* | **Certificate Course on Ward Management Module I Understanding Management Issues in the Workplace (Code No. TC-WM-0801)**<br>Organised by: College of Nursing, Hong Kong | Secretariat<br>Tel: 2572 9255 Fax: 2838 6280<br>24 CNE Points |
| **16 SUN** 8:00 pm - 10:00 pm | **FMSHK Executive Committee Meeting**<br>Organised by: The Federation of Medical Societies of Hong Kong # Council Chambers, 4/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong | Ms. Paulina TANG<br>Tel: 2527 8898 Fax: 2865 0345 |
| 8:00 pm | **Final Briefing Session of HKMA Trailwalker 2008**<br>Organised by: The Hong Kong Medical Association # HKMA Dr. Li Shu Pui Professional Education Centre, 2/F., Chinese Club Building, 21-22 Connaught Road Central, Hong Kong | Ms. Dora HO<br>Tel: 2527 8285 |
| **17 FRI** 2:00 - 5:15 pm<br>**18 SAT** 9:00 - 5:15 pm | **7th Annual Scientific Symposium on Towards Total Health**<br>Organised by: Centre of Research and Promotion of Women's Health, School of Public Health, The Chinese University of Hong Kong Speakers: Various # School of Public Health, Prince of Wales Hospital, Shatin, N.T., Hong Kong | Tel: 2252 8811 / 2252 8896<br>Fax: 2602 4360<br>Email: crpwh@cuhk.edu.hk<br>Website: www.cuhk.edu.hk/crpwh<br>CME 10.5 CNE: 10.5 |
| **19 SUN** 7:00 am | **HKMA Trailwalker Training Session VIII (Stage 1 - 5)**<br>Organised by: The Hong Kong Medical Association | Ms. Dora HO<br>Tel: 2527 8285 |
| 2:00 am | **HKMA Swimming Gala**<br>Organised by: The Hong Kong Medical Association # Hong Kong Polytechnic University, Kowloon | Ms. Dora HO<br>Tel: 2527 8285 |
| **22 WED** 8:45 am - 8:30 pm | **Clinical Updates 2008**<br>Organised by: Clinical Nurse Specialist Group (CNSG) | Secretariat<br>Tel: 2572 9255 Fax: 2838 6280<br>1-8.5 CNE Points |
| **30 THU** 2:00 pm | **HKMA Tin Shui Wai North / Yuen Long Community Network Certificate Course**<br>Organised by: HKMA Tin Shui Wai North / Yuen Long Community Network # Grand Ballroom, Harbour Plaza Resort City, 18 Tin Yan Road, Tin Shui Wai, N.T. | Ms. Jo WONG /<br>Ms. Tammy TAM<br>Tel: 2527 8285 |

## Meetings

| | |
|---|---|
| 8-9/11/2008 | **10th Beijing / Hong Kong Medical Exchange: Update on Respiratory Medicine**<br>Organised by: Hong Kong Thoracic Society, American College of Chest Physicians (HK and Macau Chapter), Hong Kong Medical Association and Chinese Medical Association# Hong Kong Convention and Exhibition Centre, Wanchai, Hong Kong, Enquiry: Secretariat Tel: 2155 8557 / 2559 5888 Fax: 2559 6910, Email: meeting.hk@asia.cmpmedica.com |
| 14-15/11/2008 | **International Symposium on Hepatology 2008 / 21st Annual Scietific Meeting**<br>Organised by: Hong Kong Association for the Study of Liver Diseases # Hong Kong Convention and Exhibition Centre, Wanchai, Hong Kong Enquiry: Secretariat: Tel: 2155 8557 / 2559 5888 Fax: 2559 6910, Email: meeting.hk@asia.cmpmedica.com |
| 21-22/11/2008 | **15th Annual Scientific Meeting - Controversies in Neurosurgery**<br>Organised by: Hong Kong Neurosurgical Society Speaker: Prof. Shigeaki KOBAYASHI # Grand Ballroom, Langham Hotel, 8 Peking Road, Tsim Sha Tsui, Kowloon Enquiry: Dr. Y.C. PO Tel: 2990 3788 Fax: 2990 3789 |
| 21-24/11/2008 | **Annual Scientific Meeting 2008 - Neuro-Genetics**<br>Organised by: Hong Kong Child Neurology and Developmetal Paediatrics # Princess Margaret Hospital and Eaton Hotel Hong Kong Enquiry: Secretariat Tel: 2155 8557 / 2559 5888 Fax: 2559 6910 Email: meeting.hk@asia.cmpmedica.com |
| 22-25/11/2008 | **2nd Asian Preventive Cardiology & Cardiac Rehabilitation Conference cum 7th Certificate Course in Cardiac Rehabilitation**<br>Organised by: Hong Kong College of Cardiology Co-Chairman: Prof. LAU Chu Pak & Dr. LAU Suet Ting Speaker: Various # Hong Kong Convention & Exhibition Centre, 1 Expo Drive, Wanchai, Hong Kong Enquiry: Secretariat Tel: 2527 8285 Fax: 2865 0943 Email: dorahkma@hkma.org Website: http://www.apccrc.com |
| 27-30/11/2008 | **Human Dignity in Modern Medicine 14th Congress of Asian Federation of Catholic Associations**<br>Organised by: The Guild of St. Luke, St. Cosmas and St. Damian Hong Kong Chairman: Dr. Peter AU YEUNG Speaker: Prof. Fr Louis ALDRICH & Prof. Luke GORMALLY # Catholic Diocese Centre, 1 Caine Road, Hong Kong Enquiry: Congress Secretariat Tel: 2363 0598 Fax: 3764 0579 Website: http://doctor.catholic.org.hk |
| 20-22/2/2009 | **CardioRhythm 2009**<br>Organised by: Hong Kong College of Cardiology & Chinese Society of Pacing and Electrophysiology Co-Chairman: Prof. LAU Chu Pak Enquiry: Secretariat Tel: 2899 2035 Fax: 2899 2045 Email: info@cardiorhythm.com Website: http://www.cardiorhythm.com |

## Courses

| | |
|---|---|
| 6,13,20,27/11/ 2008<br>4, 18/12/2008<br>8, 15, 22/1/2009 | **Certificate Course in Clinical Audit (Code No. TC-CA-0802)**<br>Organised by: College of Nursing, Hong Kong Enquiry: Secretariat Tel: 2572 9255 Fax: 2838 6280 CNE Points: 24 |
| 14/11/2008 - 16/1/2009<br>(Every Fri) | **Certificate Course on Organisation and Management in Healthcare (Code No. TC-OMH-0801)**<br>Organised by: College of Nursing, Hong Kong Enquiry: Secretariat Tel: 2572 9255 Fax: 2838 6280 CNE Points: 24 |
| 14/11/2008 - 16/1/2009<br>(Every Fri) | **Certificate Course on Palliative Care for Nurses (Code No. TC-PC-0801)**<br>Organised by: College of Nursing, Hong Kong Enquiry: Secretariat Tel: 2572 9255 Fax: 2838 6280 CNE Points: 24 |

## Upcoming Certificate Courses of the Federation of Medical Societies of Hong Kong

| Date | Course No | Course Name | Co-organiser | Target Participants |
|---|---|---|---|---|
| 7 Nov 08 - 12 Dec 08 | C136 | Certificate Course on Oral Surgery for Dental Sugery Assistant | The Hong Kong Assoication of Oral and Maxillofacial Surgeons Limited | Dental Surgery Assistant |
| 5 Nov 08 - 3 Dec 08 | C138 | 如何透過飲食和生活習慣來預防癌症 | 香港營養學會 | 有興趣人士 |
| 10 Dec 08 - 21 Jan 09 | C139 | 從食物與營養了解慢性疾病的預防 | 香港營養學會 | 有興趣人士 |

## Answer to Cinical Quiz

### Findings:

1. Splaying, cupping and irregularities are seen at distal radius and ulnar metaphysis.
2. Widened growth plates
3. Mild coarsening of bony trabeculation and decreased in bone density.
4. Bone age corresponds to ~8 yr, which is delayed.

### Diagnosis:

Ricket

**Dr. Alice Wu**
*Associate Consultant, Queen Mary Hospital.*

# 如何透過飲食和生活習慣來預防癌症

**Course No. C138**

Jointly organized by:

**The Federation of Medical Societies of Hong Kong**
**香港醫學組織聯會**

**Hong Kong Nutrition Association**
**香港營養學會**

癌症是一種影響人體多個不同器官及組織的疾病，而癌症的發展過程是複雜及並未完全被了解的。目前，每四名香港市民中，就有一位有機會患上癌症。但研究顯示，大約三分之一的癌症是可以透過健康的飲食習慣，多做運動和維持健康的體重而預防的。透過這課程，我們將會了解癌症的成因，並探討如何透過日常飲食和生活習慣來預防這疾病。

**日期** ：2008年11月5、12、19日 及12月3日
**時間** ：晚上7時至8時30分
**地點** ：香港灣仔軒尼詩道十五號溫莎公爵社會服務大廈四樓演講廳
**收費** ：每位港幣$500元(4堂)
**語言** ：粵語
**備註** ：如出席率達70%，可獲發證書

索取報名表格及查詢詳情，
請與香港醫學組織聯會秘書處聯絡或
瀏覽網址: www.fmshk.org

① **防癌飲食全面「睇」**
（講者：註冊營養師吳彥慈）
- 癌症的成因
- 飲食和癌症的關連
- 什麼食物可以有助預防癌症
- 防癌飲食要訣

② **癌症飲食誤解與真相**
（講者：註冊營養師吳彥慈）
- 常見有關飲食和癌症的謬誤
- 探討背後的真相

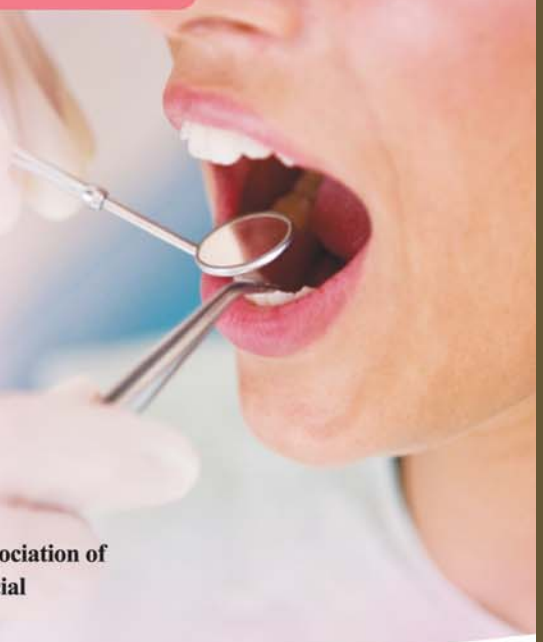
③ **運動和控制體重可以預防癌症嗎**
（ 講者：註冊營養師黃志榮）
- 運動如何有助防癌
- 運動的建議
- 肥胖和癌症的關連
- 控制體重的貼士

④ **防癌素食好「煮」意**
（ 講者：註冊營養師黃志榮 ）
- 認識素食
- 素食者的營養需求
- 素食可以防癌嗎
- 素食好「煮」意

Course no. C136

CERTIFICATE COURSE FOR GENERAL PUBLIC

# Certificate Course on Oral Surgery for Dental Surgery Assistant



A practical guide for Dental Surgery Assisting: from aseptic techniques to oral surgery for wisdom teeth and dental implant

## Jointly organised by

The Federation of Medical Societies of Hong Kong
香港醫學組織聯會

The Hong Kong Association of Oral and Maxillofacial Surgeons Limited

## Objective

Today dental practice is becoming more and more sophisticated. Technological advancement opens up more treatment options for patient. More and more oral surgical procedures are being performed in the dental office. A sound knowledge of the aseptic technique, instrumentation and understanding the different oral surgical procedures are essential for dental surgery assisting. This course aims to provide the participants an update in aseptic technique in a hospital setting that is applicable as well in a dental office. Oral surgical technique and instrumentation, eg. wisdom teeth removal, dental implant placement will be presented, the role of the dental surgery assistant will be emphasised.

### Introduction to Oral and Maxillofacial Surgery Common Oral Surgical Problems in Dental Office - Their Recognisation and Treatment

**7 Nov 08**

Speaker: Dr. Chiu Wai Kuen, Ken
Specialist in Oral and Maxillofacial Surgery

### Aseptic Techniques for Oral Surgery Procedure & Update in Sterilisation and Preparation of Instrument

**14 & 21 Nov 08**

Speaker: Ms. Chow Suk Lin, Julie
Ward Manager, Operation Theatre Services, QMH

Ms. Li Kit Ching, Phenita
Advanced Practice Nurse, Operation Theatre Services, QMH

Ms. Kong Wai Yi
Nursing Officer, Operation Theatre Services, QMH

Ms. Wong Pui Shan
Registered Nurse, Operation Theatre Services, QMH

### Minor Oral Surgery in Dental Office

**28 Nov 08**

Speaker: Dr. Chow Kiang Cheong, Ben
Specialist in Oral and Maxillofacial Surgery

### Dental Implant Update & Placing Dental Implant in Dental Office and Related Surgery

**5 Dec 08**

Speaker: Dr. Lee Kin Man, Philip
Specialist in Oral and Maxillofacial Surgery

### Medical Emergency in Dental Office, an Update and Their Prevention

**12 Dec 08**

Speaker: Dr. Lau Sze Lok, Alfred
Specialist in Oral and Maxillofacial Surgery

| | |
|---|---|
| **Date:** | 7 November 2008 – 12 December 2008 (Every Friday) |
| **Time:** | 7:00 p.m. – 8:30 p.m. |
| **Venue:** | Lecture Hall, 4/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong |
| **Language:** | Cantonese (Supplemented with English) |

| | |
|---|---|
| **Certificate:** | Awarded to participants with a minimum attendance of 70% |
| **Course Fee:** | HK$750 (6 sessions) |
| **Enquiry:** | The secretariat of The Federation of Medical Societies of Hong Kong |

**Tel.: 2527 8898** **Fax: 2865 0345** **Email: info@fmshk.org**

CME/CPD Accreditation applied for
For downloading the application form, please refer to our website: http://www.fmshk.org

# The Federation Annual Dinner 2008

31st December, 2008 (Wednesday)

***Run Run Shaw Hall***

*The Hong Kong Academy of Medicine Jockey Club Building*
*99 Wong Chuk Hang Road, Aberdeen, Hong Kong*

**Tickets are now available. Please contact the Secretariat on 2527 8898**

**THE FEDERATION OF MEDICAL SOCIETIES OF HONG KONG**
**香 港 醫 學 組 織 聯 會**

# Medical & Dental Directory of Hong Kong, 8th Edition

## Corrigendum/Updates to Medical & Dental Directory of Hong Kong (8th Edition)

| Page No. | Particulars |
|---|---|
| 442 | Qualification attained by HO Hung Kwan, Michael should read as "MB BS (**Syd**) 1994" |
| 455 | "KONG Hot Tai" should read as "KONG **Hoi** Tai" |
| 478 | "LAU The Shan" should read as "LAU **Teh** Shan" and his Chinese name should read as "劉德**譖**" |
| 519 | Qualifications attained by MING Shiu Kow should read as "MB ChB(Bristol) 1973, DRCOG 1974, **DABIM 1978**, DABFP 1978, **DABIM (Rhu) 1980, FHKCP** 1998"; and<br>His Practice should read as "Private; **Associate Professor of Medicine, The Chinese University of Hong Kong, Medicine, 1996-1998**" |
| 646 | Email Address of CHAN Wing Kin should read as "wk**a**chan@hotmail.com" |
| 658 | Qualification year attained by LI Wai Hon should read as "MB BS (HK) **1991**" |
| 716 | Tel no. of WONG Wing Kam should read as "2395 40**3**1" |
| 766 | "LEUNG Chi Tat, Anthony" should read as "LEUNG Chi Tat, **Antony**" |
| 768 | Specialty of SZE Kai Hoi, Frank should read as "**Geriatric Medicine**";<br>Practice Address should read as "**Room 2108 Wu Sang House, 655 Nathan Road, Mong Kok**";<br>Tel should read as "**2380 8827**"; and Fax should read as "**2380 8027**" |
| 774 | Practice Address of HO Sai Wah, David should read as "**3309**, Bank of America Tower, 12 Harcourt Road, Central District" |
| 776 | Practice of LAU Chu Pak should read as "Private; Honorary Professor, The University of Hong Kong, 2008-now" |
| 789 | Qualifications attained by IP Wing Kin should read as "MB BS (HK) 1982, MRCP (UK) 1990, FHKCP 1992, FHKAM (Medicine) 1995, FRCP (Lond) 1997, FRCP (Edin) 1997, **FRCP (Glasg) 2001**" |
| 838 | Chinese name of CHAN Tin Yau, Teddy should read as "陳天**佑**" |
| 872 | Practice Address of CHAN Tung Fei, Tony should read as "**10/F Wai Fung Plaza, 664 Nathan Road, Mongkok**"; and Tel should read as "**2780 0869**" |
| 875 | Qualifications attained by CHOW Hing Ping should read as "MB BS (HK) 1969, FRCS (**Edin**) 1975, FCSHK 1990, FHKAM (Surgery) 1993" |
| 885 | Mobile/Pager of LI Hak Kong should read as "71163311-994" |
| 962 | Email address of CHIU Hung Leung, Albert should read as "dralbertchi**u**@yahoo.com.hk" |
| 1028 | Qualifications attained by YU Jerome should read as "BDS (HKU) 1988, MFGDP (UK) 1996, FRACDS 1999, MSc (Dental Public Health) (Lond) 2003, DDPH RCS (Eng) 2003" |
| 1041 | Chinese name of YIP Kar Leung, Daniel should read as "**葉嘉梁**" |

# The Federation of Medical Societies of Hong Kong

## The Federation's Annual Scientific Meeting

# 2008 Cure in Cancer

**18 October 2008 (Saturday), 1:00 p.m. - 6:00 p.m.**
**M/F, Lecture Theatre, Hospital Authority Building, 147B Argyle Street, Kowloon**

- ***Advances in Colon Cancer***
  Prof. Winnie Yeo
  Department of Clinical Oncology, Prince of Wales Hospital
- ***Imaging in Cancer***
  Dr. PL Khong
  University Department of Diagnostic Radiology, Queen Mary Hospital
- ***Lung Cancer***
  Dr. James CM Ho
  University Department of Medicine, Queen Mary Hospital
- ***Genetics in the Prevention of Breast Cancer***
  Dr. Ava Kwong
  Department of Surgery, Queen Mary Hospital
- ***Breakthroughs in Breast Cancer***
  Dr. Janice WH Tsang
  University Department of Clinical Oncology, Queen Mary Hospital
- ***Radioimmunotherapy in Lymphoma***
  Dr. Rico KY Liu
  Department of Clinical Oncology, Queen Mary Hospital

**Registration Fee**
HK$100 Members of member societies
HK$200 Non-member

**Registration**
Please call our secretariat on 2527 8898 for registration form or download it from our homepage http://www.fmshk.org. Please send registration form and cheque to: The Federation of Medical Societies of Hong Kong, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong. Registration will be on first-come-first-served basis.

**CME/CPD:** Please refer to our homepage http://www.fmshk.org for details