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Current treatment and biologics in psoriasis management

Speaker: Dr. Lawrence S.W. Khoo
Senior Consultant Dermatologist, National Skin Centre, Singapore

Topical vitamin D_3 derivatives used in psoriasis include calcipotriol 50 µg/g, tacalcitol 4 µg/g, and calcitriol 3 µg/g. Calcitriol is identical to endogenous activated vitamin D. The mechanisms of action include stimulation of keratinocyte differentiation, inhibition of keratinocyte proliferation, and anti-inflammatory action.

In a left-right comparison of calcitriol ointment with vehicle, complete clearance of psoriatic lesions was achieved in 48% of sites treated with calcitriol and a further 41% showed considerable or definite improvement.

It was shown to have comparable clinical efficacy with betamethasone valerate 0.1% ointment and betamethasone dipropionate ointment. Definite improvement was found in 79% of calcitriol-treated versus 82% of betamethasone-treated patients. Greater persistence of clinical benefit was noted with calcitriol treatment. Approximately twice as many calcitriol responders were in remission for 8 weeks after treatment cessation than betamethasone-treated patients. Calcitriol ointment was shown to have equivalent efficacy to dithranol. However, calcitriol was better tolerated and accepted. Skin irritation was found in 5% of calcitriol-treated as compared to 72% dithranol-treated patients. Calcitriol ointment in combination with topical corticosteroids showed a synergistic effect with greater global improvement. It also has steroid-sparing effect because betamethasone could be used once-daily in the combination treatment instead of twice-daily in the monotherapy. Calcitriol was more effective as shown by the significantly greater global improvement ($p < 0.02$). Patients preferred calcitriol (57%) than calcipotriol (31%) ($p < 0.02$). Calcitriol was better tolerated even in sensitive areas. There was significantly less severe perilesional erythema, oedema, and stinging/burning than calcipotriol ($p < 0.02$).

In a single-centre, double blind, intra-individual comparison study of 22 psoriasis patients, calcitriol or vehicle ointment twice-a-day application was given in addition to ultraviolet B phototherapy thrice a week for six weeks. A synergistic effect was found with significantly greater global improvement with the combination treatment. In addition, there was an ultraviolet light sparing effect due to an average of 34% reduction of ultraviolet-B light exposure. There was no

significant therapeutic difference found between regimens consisting of narrow-band ultraviolet B (311 nm) therapy in combination with either calcitriol or dithranol. However, patients preferred calcitriol than dithranol in terms of quality of life and treatment acceptability. Calcitriol was safe when applied to as much as 35% of body surface area without alteration of calcium or phosphate homeostasis. In an open, long-term multicentre study, 253 patients were given calcitriol 3 µg/g twice daily for up to 18 months. There was no significant change in blood or urine calcium.

In a study that compared the combination ointment (betamethasone dipropionate and calcipotriol ointment) and ointment vehicle in patients with psoriasis vulgaris, patients receiving therapy with the two-compound product experienced fewer lesional or perilesional side effects than the calcipotriol-treated patients.

In another study, patients were given superpotent topical steroid in the morning and topical vitamin D analogue at night for the initial two to four weeks, followed by topical vitamin D analogue twice daily in later weeks for up to 12 weeks. There was no difference in global assessment of clinical success (% of clear or almost clear): 50% (in both groups) at week 2 and 79% (calcitriol), 88% (calcipotriol) at week 12 respectively.

A biologic agent is a protein derived from living sources such as human, animals, plants and micro-organisms. It is designed to alter the actions of naturally occurring proteins by inhibiting T-cell activation, target pathogenic T cells, induce immune deviation and inhibit cytokines. Types of biologic agents include recombinant proteins, monoclonal antibodies, fusion proteins, and toxin-labelled proteins.

Alefacept is a fully-human dimeric fusion protein. It has a dual mechanism of activated T-cell inhibition. In studies of using alefacept to treat psoriasis, Psoriasis Area Severity Index (PASI)-75 rates were respectively 28% with intravenous injection and 33% with intramuscular injection. In another study consisting of 31 patients (respectively 31, 28, 27 patients completed 4, 8, 12 weeks), 10 out of 31 patients experienced flu-like symptoms after the initial two to three injections. One reported buying spree. Four out of 344 patients had a CD4 count less than 250 cells/µL (lowest was 198 cells/µL) and all normalised later.

The median duration of remission (as defined as maintenance of at least 50% PASI reduction in those who have reached PASI-75) after one 12-week course of intravenous alefacept was 216 days while that for intramuscular alefacept was 209 days. Alefacept produced significant improvement in quality of life. Chill was the only adverse effect with incidence greater than 5%. No increase in risk of malignancy was apparent after six courses of alefacept treatment.

Etanercept consists of the fusion of two naturally occurring tumour necrosis factor (TNF) receptors, linked to human immunoglobulin. It binds to TNF, rendering it biologically inactive, and thus reducing inflammation in multiple diseases such as psoriasis. Significant PASI responses were noted after 12 weeks of treatment. Sustained PASI 75 followed dose reduction and sustained benefit were demonstrated for treatment up to 48 weeks. Patients' quality of life significantly improved within 2 weeks.

Efalizumab saturates binding sites on T-cells without depleting lymphocytes and blocks the binding of T-cell leukocyte function antigen-1 to the intercellular adhesion molecule-1 on antigen-presenting cells, vascular endothelial cells, and keratinocytes. Efalizumab inhibits T-cell activation in the lymph nodes and disturbs the trafficking of T-cells to the dermis and epidermis. It also inhibits T-cell reactivation in the dermis and epidermis.

A total of 2335 psoriasis patients were included in safety database, consisting of 1620 efalizumab-treated and 715 placebo-treated patients. This was one of the largest safety cohorts for biologic psoriasis therapy to date, in randomised, placebo-controlled trials. The safety profile for efalizumab was consistent

across all trials. No end-organ toxicity has been observed in patients receiving efalizumab. Elevations in alkaline phosphatase (4% of efalizumab-treated patients) had been observed in clinical trials.

Efalizumab is best used as a continuous therapy. It has a reversible effect upon T-cells. Recurrence of disease is expected upon discontinuation and the median time to relapse is 64-70 days. In clinical trials, approximately 3% of patients experienced rebound of disease which could be more than 25% of baseline. New morphologies developed in some patients. Rebound is more likely to occur in patients who did not achieve PASI 50 during treatment. Rebound was also seen in 11.1% of placebo-treated patients. Rebound can be managed by re-treatment with efalizumab or other psoriasis therapies.

Infliximab is a chimeric anti-TNF-alpha monoclonal antibody. When infliximab was given intravenously at a dose of 5 mg/kg, 10 mg/kg or placebo at week 0, 2 and 6, the PASI-75 rates were respectively 82%, 73% and 18% at week 10.

Adalimumab is a fully human monoclonal antibody which is specifically directed against TNF. When administered in long term combination with methotrexate or as monotherapy, it was found to be well-tolerated and with a low incidence of allergic reactions (< 1%). It is indistinguishable from human IgG1 – with a half-life of approximately 14 days. It is administered subcutaneously by a prefilled, ready-to-use syringe specifically designed for patients with rheumatoid arthritis.

Learning points:

Calcitriol ointment when used singly or in combination with other agents is an useful option in the treatment of psoriasis. Nowadays, a number of biologics are also found to be useful in the management of psoriasis.

Eczema and psoriasis: the current treatments and the outlook into biologics

Speaker: Dr. David Orchard
Paediatric Dermatologist, Dermatology Department, Royal Children's Hospital, Melbourne, Australia

In the management of eczema, it is wise to find out the triggering factors for eczema flares in that particular child and settle active eczema with immunosuppressive therapies, including topical corticosteroids, topical calcineurin inhibitors, ultraviolet light therapy, oral prednisolone, cyclosporine A, other immunosuppressants, and possibly biologics. However, with more options for immunomodulation, dermatologists tend to minimise the critical importance of managing eczema triggers, such as dryness, heat, irritation, infection, allergy, food intolerance, and other immune stimulus.

When dryness is the trigger factor, one should avoid the use of drying agents. Bath oil, soap substitutes and moisturisers should be used and tailored to individual's requirements and lifestyle. If heat is a trigger factor, one should keep bath or shower tepid only, dress appropriately, minimise sweating at night and use wet dressings.

Patients should avoid further irritation by lotions, potions, medicaments, soaps, detergents, shampoos and environmental irritants such as sand, wool, clothing seams and tags, and chlorine. Soap substitutes can be used instead. The use of barrier creams on cheeks and napkin area is also helpful.

Immune stimulation can trigger eczema flares, including viral infections, bacterial infections, vaccinations, stress, and urticaria. Antibiotics should be given for superimposed staphylococcal infection. Bath time is the best time to remove crust in children. Topical antiseptics may cause irritation.

Features suggesting a role of environmental allergen include: 'exposed area' distribution, nocturnal pruritus, and toddler or childhood onset. Features suggesting a role of dietary allergen include: an infant less than 12 months old, widespread background erythema, baby unsettled because of itch, scratching of normal-looking skin, and a history of sudden severe widespread flares. The features suggesting food 'intolerance' include: a child between 18 months old and 5 years old; perioral, hand and napkin dermatitis. The culprit food is usually high in salicylates and amines such as tomatoes, strawberries, citrus fruits, vegemite, acidic preservatives.

Topical corticosteroids are used to clear eczema and should be stopped after the "burst" rather than used as daily maintenance. Topical corticosteroids should be prescribed in adequate potency and in enough quantities.

Topical pimecrolimus and tacrolimus are calcineurin inhibitors which work as well as mild to medium strength corticosteroids. Their onset of action is slower than topical corticosteroids. They may cause irritation. There are no known long term local side effects. However, there are concerns about the systemic absorption if large body surface area is covered. Topical tacrolimus and pimecrolimus are used in recalcitrant facial eczema, stretch-mark areas, perioral dermatitis/ rosacea, respite from topical steroids, and patients with steroid phobia.

To maximise compliance, it is useful to apply topical treatments two times per day, use strong topical corticosteroid on active areas and moisturisers on other areas, alleviate irrational fear regarding steroids, bargain with teenagers, keep looking for true eczema precipitants, and admit defeat when stronger therapies are required.

The role of biologics in eczema is thought to shift the axis from TH1 lymphocytes to TH2. There is a potential role of cytokine blocking agents.

Psoriasis differs from eczema that triggering factors are only occasionally identified, such as streptococcal infection and other infections and stress.

Therapy is primarily suppressive. It is important to let patients aware of this. The success of management depends on targeting the right therapies to the right patient. In psoriasis, the philosophy of therapy is 'aim to clear', employing combination therapies with aggressive 'treatment on' phases followed by rests or maintenance phases. Sometimes, it may be necessary to rotate therapies for more severely affected patients.

Therapies work through different mechanisms and are additive in combination. Many therapies only give moderate and therefore insignificant improvement if used in isolation. Combination therapies may reduce the potential of side effects from each individual therapy. Rotation of therapies will play a key role in the therapy of those patients with more severe disease. This allows newer options for refractory patients.

Learning points:

Eczema is a multifactorial condition and physicians should not overlook the primary strategy of managing the underlying precipitants. In psoriasis, the philosophy of therapy is 'aim to clear' by using combination therapies with aggressive 'treatment on' phases and rotational therapies.

Long-term safety – 12 years of evidence with tacrolimus ointment

Speaker: Prof. Roger Allen
Consultant Dermatologist, Department of Dermatology, Royal Children's Hospital, United Kingdom

Tacrolimus was the first topical calcineurin inhibitor developed for the treatment of atopic dermatitis. To date, more than 30 clinical studies have

investigated the efficacy and safety of tacrolimus ointment in 16,000 atopic dermatitis patients including 3,000 children. More than 35 million prescriptions have been written for tacrolimus ointment in Europe. This presentation reviewed the clinical data concerning the safety of topical tacrolimus.

Burning sensation was a common side effect. It was reported in 60% of adults and 20% of children during the initial application. In a randomised, double blind, multi-centre study, 0.03% or 0.1% of tarcolimus ointment were used on 1,414 patients with moderate to severe atopic dermatitis. In both adults and children, the most common adverse events were burning sensation, pruritus and erythema, which were limited to the site of application. These side effects were reported to be mild to moderate in severity, were transient (last for 15-20 minutes) and usually occurred during the first few days of treatment.

The long term safety and tolerability of 0.03% and 0.1% tacrolimus ointment in children was also studied. In a study, 466 children, of aged 2-15 years, with moderate to severe atopic dermatitis, were treated intermittently or continuously with either 0.03% or 0.1% tacrolimus ointment for at least one year. The drug was well tolerated. The most common adverse effects were burning sensation (26.6%), pruritus (26.4%) and skin infection (16.1%). The majority of the events were limited to the site of application, mild to moderate in severity, transient and rarely leading to treatment discontinuation.

One of the major concerns about the use of topical tacrolimus was the risk of infection. According to a 6-month, double-blinded study comparing tacrolimus ointment with topical corticosteroids, the incidence of application-site skin infections was low and comparable to topical corticosteroids. The incidence of herpes simplex infection did not increase over time. Another study also showed a low incidence (< 13%) of application-site infections for a period of three years in adults and children.

The concern about malignancy was also discussed. The incidence of non-melanoma skin cancer in patients using topical tacrolimus showed no difference from the general population. Although cases of lymphoma were reported among patients using tacrolimus ointment, there was no evidence to prove the causal relationship between the use of topical tacrolimus and malignancy.

In summary, clinical data over the past 12 years on using tacrolimus for treatment of atopic dermatitis showed that it was a safe drug and was well tolerated by both adults and children.

Learning points:

Tacrolimus ointment is considered to be safe and effective in treatment of moderate to severe atopic dermatitis in both adult and children. The long term safety profile should be further studied as it is still a relatively new drug.

Evaluation of the irritancy potential of adapalene and tretinoin in volunteers of different ethnic origins

Speaker: Prof. Chee-leok Goh
Consultant Dermatologist, National Skin Centre, Singapore

Topical retinoids have been widely used for acne vulgaris since tretinoin was first shown to be useful in treating skin disorders with abnormal keratinization in early 1960. The speaker emphasised that topical retinoids are effective for both inflammatory acne and comedones. Apart from reversing the abnormal keratinization, some topical retinoids have effect on inflammation by modulating the immune response, inflammatory mediators and the migration of inflammatory cells. A study done by Shalita et al showed a 50% reduction of inflammatory and non-inflammatory

lesions at week 12. The main side effect of topical tretinoin is skin irritation with erythema, dryness and scaling which is dose and vehicle dependent. Different preparations are reported to have different irritation potential.

A study was carried out in Singapore comparing the cumulative irritancy potential of adapalene 0.1% gel and tretinoin 0.025% gel following applications to the face and forearms of volunteers from different ethnic origins. Volunteers were randomised to apply each product daily to one or the other half-face for 21 days. On the forearms, products were applied under occlusion for four days. Participants were reviewed on day 3, 7, 10, 14, 17 and 21. Criteria for evaluation were signs and symptoms on the face (erythema, desquamation, dryness, stinging/burning, pruritus) and forearms (irritation, stinging/burning, pruritus and biophysical measurements including colorimetry and trans-epidermal water loss). A total of 73 volunteers from four ethnic groups (Chinese, Europeans, Indians and Malays) were recruited. Adapalene was significantly better tolerated by all ethnic groups than tretinoin on the face and forearms. Chinese were most susceptible to develop irritation, followed by Indians, Malays and Europeans.

In conclusion, Adapalene 0.1% gel showed a better cutaneous tolerability on the face and forearms than tretinoin 0.025% gel for all four ethnic groups. An inter-ethnic difference in the irritation susceptability could be observed.

Learning points:

Topical retinoids are effective in both inflammatory and non-inflammatory lesions of acne vulgaris. Different topical retinoids have different irritation potential and Chinese are more susceptible to cutaneous side effects.

Laboratory diagnosis of bacterial sexually transmitted diseases

Speaker: Dr. Kai-man Kam
Consultant Medical Microbiologist, Public Health Laboratory Centre, Centre for Health Protection, Department of Health, Hong Kong

The presumptive identification of Neisseria gonorrhoeae is based on the morphology. It is a Gram-negative diplococci and is oxidase-positive. Confirmatory identification can be made by cystine trypticase agar sugar test. It determines acid production from carbohydrates in cystine trypticase agar, using phenol red as indicator: yellow as positive while red or orange will be negative. More sophisticated tests will be used when suspected isolates fail to produce acid from glucose. These tests may play a role in confirming gonorrhoea infection at extragenital sites in low-risk patients, in potential medico-legal cases or in doubt of the identity of the isolate.

Agar dilution method is used to test for the antibiotic sensitivity of Neisseria gonorrhoeae. A breakpoint plate minimal inhibitory concentration method is detected against penicillin, ofloxacin, tetracycline, spectinomycin and ceftriaxone. These particular antimicrobial agents are included in line with the surveillance programme of World Health Organization. Ceftibuten was not included because there is no reference range to define resistance and susceptibility. However, ceftibuten may be added in the future if there are more resistance cases. The other sensitivity tests include disk diffusion method and beta-lactamase test.

COBAS Amplicor CT is a polymerase chain reaction (PCR) test to detect chlamydia trachomatis. It has sensitivity ranged from 82% to 98% and specificity greater than 99% for urethral smear samples. Up to 66 patients' specimens can be tested in one day on one COBAS Analyzer. The Amplicor specimen transport medium can be stored at room temperature for up to 10 days.

Syphilis testing algorithm in the Public Health Laboratory Centre begins with a Treponemal-based screening: enzyme immunoassay tests (EIA). It is sensitive at all syphilis stages and is specific. It is automated for mass processing and the test interpretation is objective. The non-treponemal tests fail to detect very early or late stage of syphilis or in some human immunodeficiency virus-infected cases. There can be a problem with prozone phenomenon and the biological false positive rate is reported to be 1-2%.

The test results of a routine 4595 consecutive sera from antenatal clinics showed that the EIA method had sensitivity of 100% and specificity 99.7% while the Venereal Disease Research Laboratory (VDRL) test had 34% and 99.9% respectively. The positive predictive value and negative predictive value for EIA were 80.6% and 100% respectively for EIA and 89.5% and 99.3% for the VDRL test.

Treponema pallidum Western blot test is currently under evaluation. It is the first syphilis immunoblot technique to validate the probable antigens as diagnostic indicators.

Bacterial vaginosis is characterised by a shift in the vaginal flora from the dominant flora of Lactobacillus species to mixed vaginal flora including Gardnerella vaginalis, Bacteroides pecies, Mobiluncus species, and Mycoplasma hominis. The presence of clue cells greater or equal to 20% of epithelial cells is considered as significant. If clue cells are less than 20%, then we need to examine different bacterial morphotypes according to Nugent's criteria. Nugent's score of 7-10 is considered as significant.

Trichomonas vaginalis is the most prevalent non-viral sexually transmitted diseases in the world. Trichomonas can be detected after incubation in Feinberg medium for two days, a wet mount is prepared and examine under microscope. This is still considered as the "Gold standard method". Other detection methods consist of monoclonal-antibody-based enzyme-linked immunosorbent assay and molecular methods using probe hybridization, PCR and real-time PCR assays.

Many methods have been developed for detecting Mycoplasmas and Ureaplasmas, including culture, antigen detection, DNA probes and PCR. The latter is used by the speaker. Susceptibility test of antibiotics including doxycycline, ofloxacin, erythromycin, tetracycline, ciprofloxacin, azithromycin and clarithromycin can also be performed.

Finally Dr Kam reminded us to take specimens carefully: "Optimal specimens, Optimal results".

Learning points:

Microbiological testing for sexually transmitted infections consists of detection of pathogens and antimicrobial susceptibility tests. To obtain optimal test results, we have to liaise closely with the laboratory staff, take specimens carefully as well as to interpret the results with caution. Molecular techniques are on the horizon but good quality control is required.

HIV testing – what do we need to know

Speaker: Dr. Ka-hing Wong
Acting Consultant, Special Preventive Programme, Centre for Health Protection, Department of Health, Hong Kong

Over the past two decades, advent of effective treatment and new tests against human immunodeficiency virus (HIV) infection has rendered HIV testing very important in both clinical management and prevention strategies.

HIV antibody testing is the gold standard for diagnosis of HIV infection. The standard means of testing is to perform screening using the extremely sensitive but relatively less specific

enzyme-linked immunosorbent assay (ELISA) test. In cases of positive ELISA, a confirmatory test should be performed, usually by Western blot technique. The most important antibodies are those against the envelope glycoproteins such as gp120, gp160, and gp41. The p24 antibody is usually present but may be absent in the later stages of HIV infection.

Testing for plasma HIV-1 RNA is performed for (1) monitoring of disease progression and treatment response in known infected, (2) acute retroviral syndrome, (3) perinatal infection, and for (4) assessment of the probability of transmission.

It is noteworthy that there are some differences between HIV testing for the clinical and epidemiologic surveillance setting. For the clinical setting, it is important to perform test in patients who (1) have history at risk (unsafe sex, unsafe drug injection), (2) clinical suspicion of HIV-related symptoms/diseases, notably sexually transmitted infection (STI), or (3) persons who have been sexually assaulted or have occupational exposure. For public health screening purposes, HIV tests are performed routinely in antenatal, pre-donation, and methadone clinic attendees.

The development of new tests for HIV creates new prospects for expanding HIV testing to identify and treat HIV-infected persons earlier. The OraQuick® HIV rapid test (OraSure Technologies, Inc., Bethlehem, Pennsylvania) was approved by the Food and Drug Administration in November 2002. The rapid HIV test is simple, provides HIV test results in 20 minutes, can be stored at room temperature, requires no special equipment except those for a finger-prick, and can be performed outside clinical settings. However, HIV-positive test results will still require confirmation by Western blot or immunofluorescence assays.

Because of the potential public health benefits of rapid HIV testing, the Centers for Disease Control and Prevention of the United States have advocated HIV tests as a routine for all medical consultations. The initial experience has shown that routine and voluntary HIV screening for all sexually-active patients in the general population may be cost-effective.

The primary care doctors have therefore a revised role to play in the expanded HIV testing strategies. They are involved not only in the screening and treatment of STIs, but also promoting HIV awareness and protection (use of condom for safer sex), detection of HIV positive individuals, counselling of infected patients, reporting of cases to the Department of Health (using the Form DH 2293), as well as partner counselling and referral.

Learning points:

HIV antibody testing is the gold standard for diagnosis of HIV infection which consist of screening test by ELISA and confirmed by Western blot. Rapid HIV testing is now available and can serve for special clinical indications. The primary care doctors have therefore a revised role in the expanded HIV testing strategies, including screening, treating concomitant STIs as well as counselling.

Darier's disease: a study of 32 cases in Hong Kong

Speaker: Dr. Y.H. Chan
Medical and Health Officer, Social Hygiene Service, Department of Health, Hong Kong

Darier's disease (DD) or keratosis follicularis is a rare cutaneous disease with an autosomal dominant mode of inheritance. Recent studies show that the underlying defect is the result of mutations in the ATP2A2 gene on chromosome 12q23-24 that encodes for a sarco/endoplasmic reticulum calcium ATPase pump (SERCA 2) expressed on human skin and mucosa.

A manual search of skin biopsy records in Social Hygiene Service from 1983 to 2003 was performed. Records with keywords DD, keratosis follicularis or acantholytic dyskeratosis were retrieved. Demographic and clinical data were collected from 32 DD patients. Quality of life in these DD patients was assessed with the use of Dermatology Life Quality Index (DLQI). ATP2A2 gene mutation analysis was carried out in all DD probands and affected family members.

Of the 32 Chinese patients studied, there were 15 males and 17 females and the mean age of onset was 15. Twenty patients had positive family history. The estimated incidence of DD in Hong Kong was 0.025 per 100,000 per year, which was lower than that in other European countries. The commonest presentation was greasy hyperkeratotic papules, followed by verrucous plaques. The disease most commonly started on the face (50%), followed by the neck (13%). Common acral manifestations included palmar pits, V shaped nicks, nail ridging, brittle nails and subungual hyperkeratosis.

Pruritus was common (75%) and malodour was present in 28% of patients. Secondary bacterial, fungal and herpes simplex infection were present in 66%, 19% and 9% of patients respectively. Ninety percent of patients reported heat, sweating or sunlight as aggravating factors. Others reported stress, menstruation and high humidity as contributory factors to disease aggravation. Most patients lived with the disease without major problems.

The average DLQI score was 6.43 with the majority (27/28=96%) scored less than 15. Focal acantholytic dyskeratosis with corps ronds and grains were the usual histopathological findings. Systemic retinoid was the most effective therapy for our patients although minor side effects were common.

In this group of DD patients, four novel mutations were found, which included three frameshift insertions/deletions and one intron splice site mutation. In our locality, frameshift insertion or deletion was the commonest form of mutation (75%) whilst missense mutation was the commonest in reports from Japan, Taiwan and the United States of America. No mutation hotspots and clear-cut genotype-phenotype association could be identified.

Learning points:
Darier's disease is as a result of mutations in the ATP2A2 gene. Frameshift insertion or deletion is the commonest mutation in local Chinese patients with Darier's disease.

Cutaneous melanoma: epidemiology in Hong Kong

Speaker: Dr. S.K. Hui
Medical and Health Officer, Social Hygiene Service, Department of Health, Hong Kong

Cutaneous melanoma is an important disease entity for its potential fatality and its urgency for timely management. The incidence of cutaneous melanoma had substantially increased among all Caucasian populations in the last few decades. The mortality of melanoma had also been rising between 1940 and 1990 in most parts of the world, though at a pace slower than that of incidence rates. Due to the increase in incidence and the subsequent mortality, cutaneous melanoma had become a significant and growing public health burden in western countries.

Between 1983 and 2002, the mean incidence of melanoma in Hong Kong was 0.8/100,000 per year while the world age standardised rate was 0.7/100,000 per year. The male to female ratio of newly diagnosed melanoma cases was 1.06:1. The incidence of cutaneous melanoma in Hong Kong was double than that of Japan and triple than that of mainland China but it was lower as compared with Caucasians. The

incidence in Hong Kong between 1983 and 2002 showed a modest decreasing trend, while the mortality of melanoma showed an increasing trend within the period. These changes might reflect the racial changes among the local population around 1997. In Hong Kong, the case fatality for cutaneous melanoma was high (43% for male and 34% for female), it was ten times higher than that of non-melanoma skin cancer. Male sex and aging were the two poor prognostic factors. Males had a higher incidence, mortality and case-fatality rates. The crude incidence and mortality rates showed a steep increasing curve with age.

Similar to other studies in Asian populations, the feet were the commonest site of predilection of cutaneous melanoma in Hong Kong. It accounted for about 50% of cases according to a review done in Social Hygiene Service and five major hospitals in Hong Kong. Since the feet were not commonly exposed to ultraviolet light, further studies were needed to identify aetiologic factors, other than ultraviolet light, in melanomas in Asian population. Acral lentiginous melanoma was the commonest pathologic type.

Since early detection of primary cutaneous melanoma in its thin early phase remains the best chance for cure, dermatologists are at the forefront of this effort.

Learning points:

The incidence in Hong Kong between 1983 and 2002 showed a modest decreasing trend, while the mortality of melanoma showed an increasing trend. Early melanoma detection is important for disease management.

Health-related quality of life among Chinese people with psoriasis in Hong Kong

Speaker: Dr. C.T. Tse

Medical and Health Officer, Kowloon Integrated Treatment Centre, Department of Health, Hong Kong

Psoriasis is a common skin disease in Hong Kong. It ranked as the fifth most common skin disease in 2001 in the Social Hygiene Service. Its effect on health-related quality of life (HRQOL) is well documented in the western literatures. A study was carried out in the Social Hygiene Service, aiming at describing HRQOL in psoriasis patients in local Chinese and examining the relationship between HRQOL and clinical severity. Chinese adults (aged 18-65 years old) with psoriasis for more than one year were asked to complete the Chinese (Hong Kong) SF-36 health survey. The SF-36 scores were reported after age- and sex- specific standardisation of Hong Kong normative values. Concurrently, the clinical severity was measured by the attending doctors, using Modified Psoriasis Activity and Severity Index (MPASI).

Of the 132 Chinese patients recruited, 94 were male (71%). The mean age was 41.3 years old and 95% had chronic plaque psoriasis. The greatest self-reported disability, assessed by SF-36, was the impairment in social functioning. Both the SF-36 physical composite score and mental composite score were significantly lower than that of the sex- and age-matched Hong Kong healthy controls. This reduction of physical and mental functioning in psoriasis was comparable to that of Severe Acute Respiratory Syndrome (SARS) or bronchiectasis. Gender, age group, engagement in work/study and duration of psoriasis did not have any association with HRQOL. The physical composite score in psoriasis patients with arthropathy was lower that those without joint involvement. The SF-36 summary scores had only weak correlations with MPASI.

This study confirmed the negative impact of psoriasis on HRQOL among local Chinese people. The degree of disability experienced by people

with psoriasis was comparable to that of people with SARS or bronchiectasis. Therefore the impact of psoriasis on patients should not be trivialized.

The weak correlation between HRQOL and MPASI suggested that patient-reported HRQOL and physician-assessed clinical severity were two independent outcome measures. Both clinical severity and quality of life should be used as outcome measures in clinical trials of psoriasis.

Learning points:
The impact of psoriasis on quality of life of patients cannot be judged solely on the basis of objective psoriasis severity scoring. Both clinical severity and quality of life should be used as outcome measures in clinical trials of psoriasis.

Timing for the treatment of Stevens-Johnson syndrome and toxic epidermal necrolysis with intravenous immunoglobulin

Speaker: Dr. C.K. Yeung
Medical Officer, Department of Medicine, Queen Mary Hospital, Hong Kong

Toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS) are acute, life-threatening cutaneous reactions mostly related to medications. The mortality rates of TEN range from 16% to 30%. The Fas blocking antibodies in intravenous immunoglobulin (IVIG) that block Fas-FasL interaction may inhibit the disease process. A retrospective case-control study was carried out to evaluate the effect of timing of IVIG therapy in TEN and SJS on disease progression and mortality.

The study included six TEN or SJS patients who received IVIG and 10 historic controls. Objective responses to IVIG, survival at day 45, IVIG tolerance were assessed. Majority of the TEN and SJS were drug induced, the most common culprit was allopurinol, which was followed by anticonvulsant. Six consecutive patients (TEN = 4 and SJS = 2) with a mean body surface area (BSA) involvement of 45% (range: 10-90%) received IVIG treatment 1 g/kg daily for three days at a mean of 3.3 days (range 1-7 days) after disease onset. The control group consisted of four TEN and six SJS patients with a mean BSA involvement of 25% (range: 10-60%). There was no statistical difference in age and BSA involvement between case and control.

One patient who received IVIG died (mortality 16.7% for the IVIG group) while the SCORTEN score predicted 2.3 deaths (37.6%). The deceased patient had been given IVIG seven days after the onset of eruption while all surviving patients received IVIG within four days of eruption. Earlier therapy seemed to associate with a better outcome. Interruption of further skin detachment occurred after 4.0 ± 1.9 days and complete wound healing took an average of 9.2 ± 2.5 days after institution of IVIG. No side effects were observed in the IVIG group. In the control group, one patient died (mortality 10% for the control group). The cessation of further detachment occurred after 5.3 ± 1.6 days and complete wound healing took an average of 11.2 ± 3.3 days in the control group. Statistical comparison did not show any significant difference in timing for cessation of further skin detachment and complete wound healing between the case and control, possibly related to the small sample sizes in both groups.

As most damage to the epidermis likely occurs in the first four to six days after onset of skin eruptions, benefits of any therapy can only be elicited if it is given early. Early administration of IVIG seems to be useful and safe for TEN and SJS.

Learning points:
IVIG is a useful and safe therapy for TEN and SJS and early administration seems to be associated with a better outcome.