• Recent Advances in Cosmetic Dermatology
  Dr Chan Hin Lee, Henry (陳衍里醫生)

• The Use of Topical Drug Therapy in Atopic Eczema
  Dr Chan Pui Yiu, Nicola (陳珮瑤醫生)

• Cutaneous Manifestations of Internal Diseases
  Dr Yeung Chi Keung (楊志強醫生)
## Criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Topical</th>
<th>Oral</th>
<th>Combination</th>
<th>Nail removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Involvement &lt; 50% nail plate</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Minimum number (3 or 4) of nails involved</td>
<td>✔</td>
<td>✔</td>
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<tr>
<td>3. Unable to swallow pills</td>
<td>✔</td>
<td>✔</td>
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<tr>
<td>4. No melanonychia</td>
<td>✔</td>
<td>✔</td>
<td></td>
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<tr>
<td>5. Known drug interaction/allergy</td>
<td>✔</td>
<td>✔</td>
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<tr>
<td>6. Mycological exam – causative fungi known drug interaction/allergy</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
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<tr>
<td>7. &gt;50% nail involvement</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
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<tr>
<td>8. Matrix area involvement (25.84% of cases in the recent EUROO study)</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>9. Topical drug penetration suboptimal</td>
<td>✔</td>
<td>✗</td>
<td>✔</td>
<td>✗</td>
</tr>
</tbody>
</table>

*After nail removal

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**References:**
6. Evans EDV et al. Data on File

Prescribing information available on request.
Galderma Hong Kong Ltd. Tel: 2824 0333 Fax: 2827 7760
Unit 1401, 14/F, Ming An Plaza, Phase 1, 8 Sunning Road, Causeway Bay, Hong Kong.
In this special dermatology issue, three contributors write on a range of topics that cover both the medical and cosmetic aspects of dermatology. Dr Yeung Chi Keung’s article on cutaneous manifestations of systemic diseases aims to refresh our readers in this important area of dermatology. Dr Nicola Chan’s article focuses more on the topical management of atopic dermatitis. Finally, Dr Henry Chan’s article updates readers on the new advances of cosmetic dermatology. We hope that this issue will prove to be of interest to our readers.
Recent Advances in Cosmetic Dermatology

Introduction

In recent years, there has been much advance in cosmetic dermatology, especially in the areas of fractionated skin rejuvenation and noninvasive body contouring. This article will address these two areas of recent interest and their application in Asian patients.

Fractionated Skin Rejuvenation

Fractional photothermolysis is a new concept of cutaneous remodelling, whereby lasers are used to induce zones of microscopic thermal injury that consist of marked areas of tissue denaturation 50 to 100 microns in diameter, which are surrounded by normal viable tissue. As the area of thermal injury is very small, the lateral migration of keratinocytes occurs rapidly, which leads to the complete re-epithelialization of the epidermis within 24 hours. By taking into consideration the mismatch between the epidermal and dermal healing processes, fractional photothermolysis allows skin rejuvenation to be achieved with a minimal risk of complications and a high degree of efficacy.

During each treatment session, a variable ratio of the skin surface is treated, the extent of which is primarily determined by the density settings of the device and the number of passes. Usually, about 16% to 32% of the skin surface is targeted per treatment session.

Fractional photothermolysis is a new concept of cutaneous remodelling, whereby lasers are used to induce zones of microscopic thermal injury that consist of marked areas of tissue denaturation 50 to 100 microns in diameter, which are surrounded by normal viable tissue. As the area of thermal injury is very small, the lateral migration of keratinocytes occurs rapidly, which leads to the complete re-epithelialization of the epidermis within 24 hours. By taking into consideration the mismatch between the epidermal and dermal healing processes, fractional photothermolysis allows skin rejuvenation to be achieved with a minimal risk of complications and a high degree of efficacy.

Ablative fractional resurfacing involves the use of ablative lasers (carbon diode or Erbium:YAG) not only to coagulate, but also to vaporize the central zone of the target tissue. Several factors determine the amount of tissue injury and depth of penetration, including the power density, pulse duration, and the type of laser. As the volume of tissue that can be removed after a single treatment session covers up

Key words: Cosmetic dermatology (醫學美容), fractionated technology (分段技術), cryolipolysis (冷凍熔脂術)
to 45% of the target area, the procedure is associated with substantial down time. Swelling can last for 1 week and erythema for another 3 weeks. Ablative fractional resurfacing can be effective in the treatment of severe photoageing, skin laxity, atrophic acne and surgical scars. The main advantages over nonablative fractional resurfacing are that only a single treatment session is necessary, and that it can improve skin laxity due to the removal of a volume of tissue.5 (Figure 1) In Asians, the risk of PIH is significant, and more than 50% of patients may experience the complication. The risk of PIH can be reduced by lowering the laser settings. However, this reduces the efficacy of treatment so that multiple treatment sessions will be necessary. In this case, there is little advantage over nonablative fractional resurfacing. Appropriate patient selection is important for obtaining good clinical outcome. Male patients with acne scarring or photoageing and female patients with a significant degree of skin laxity who are reluctant to have more invasive surgical procedures are ideal candidates for ablative fractional resurfacing.

Fractional radiofrequency has recently been developed as another form of fractionated ablative skin rejuvenation that can be effective if the appropriate patient is selected for the procedure. More studies are necessary to determine its role in Asian patients.

Recently, focused ultrasound has been shown to induce deep thermal tissue injury with a depth of as much as 3 to 4.5 mm.6 The epidermis is spared, making it an ideal tool for Asians. Our recent work looking at its application in Asians indicated its safety, but optimal parameters for improved efficacy are yet to be determined. The device is still pending approval by the US FDA and, therefore, its use remains experimental at this stage.

Noninvasive Body Contouring

While liposuction remains the gold standard for improvement of body contour, the potential adverse effects and down time associated with the surgical procedure has led to intense research in the development of noninvasive means to enhance body contour. Various methods have been tried in recent years, including chemical-induced lipolysis, devices to induce thermal or mechanical injury of the adipose tissue, and, more recently, cold-induced lipolysis (cryolipolysis). Chemical-induced lipolysis involves the injection of chemicals such as phosphatidylcholine combined with its emulsifier, deoxycholate, into the adipose tissue.7 Recent studies indicated...
that lipolysis occurred as a result of the detergent action of deoxycholate. As the effect is nonspecific, liver derangement may also occur. As a result of these adverse effects, many countries, including the United Kingdom, Korea and Singapore, have now banned the use of the substance for cosmetic purposes.

Several medical devices, including laser, focused ultrasound and radiofrequency, can induce thermal injury to the adipose tissue. However, the approach is not an ideal option for improvement of body contour as it is not selective and is associated with pain. More recently, focused ultrasound has been used to mechanically rupture adipose tissue. While early studies did demonstrate efficacy, such result has not been found to be consistent.8

Cryolipolysis is the use of heat extraction to induce crystallization of triglycerides within adipose cells.9 As the freezing points of water and triglyceride are different, water, which is the main component of other cells, is not affected. When the application of heat extraction is removed, body temperature warms up the triglycerides, which then return to liquid state. The change in state of triglycerides from liquid to solid and then back to liquid has been hypothesized to cause apoptosis of adipocytes, which occurs gradually over 2 to 6 months. A recent study showed a normalized fat layer reduction of 20% after 2 months, and 25% after 6 months.10 Adverse effects are mild and transient, including bruises caused by the suction applicator, mild numbness that lasted for an average of 3 weeks, and mild abdominal discomfort.

In the author’s experience, good results can be obtained with appropriate patient selection. (Figure 2)

**Conclusion**

In conclusion, fractionated skin rejuvenation has led to successful treatment of wrinkles, scars and, more recently, skin laxity. Cryolipolysis is a novel method of noninvasive fat removal.

**References:**

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- Highest glucocorticoid receptor affinity* and greatest glucocorticoid receptor selectivity*9
- More prolonged anti-inflammatory effect*9

*Statistically significant nasal and ocular symptom improvement in all SAR studies1,3

AVAMYS™ is also innovative
- Novel delivery system with patient-preferred sensory attributes4,6,7
  - No smell, alcohol-free, minimal or no aftertaste4,5
  - Fine Mist4
  - Lowest spray volume (half of other INS) to ensure little or no drip down throat4,5
  - Side actuation for easier administration4

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* Compared to fluticasone propionate, mometasone furoate, ciclesonide AP, budesonide, dexamethasone
* Compared to fluticasone propionate, mometasone furoate, ciclesonide AP, budesonide
* Compared to fluticasone propionate, mometasone furoate
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References:
The Use of Topical Drug Therapy in Atopic Eczema

Dr Chan Pui Yiu, Nicola
(MBBChir (Cantab), MRCP (UK), FHKCP, FHKAM(Med)
Specialist in Dermatology
Honorary Clinical Assistant Professor,
Department of Medicine,
University of Hong Kong

Key words:
Atopic eczema (異位性濕疹), emollients (潤膚霜), topical corticosteroids (外用類固醇), topical calcineurin inhibitors (外用免疫抑制劑)

Atopic eczema (AE) is a common chronic inflammatory skin condition associated with pruritis, dryness, erythema, scaling and exudation. The pathogenesis of AE involves the interplay of genetic, immunological and environmental factors. Skin barrier dysfunction, primary epithelial defect with aberrant immunological responses to microbial infection and allergen exposure all play a part in the complex pathophysiology of AE.

The aims of AE treatment are to avoid any triggering factors, to restore and strengthen skin barrier function, as well as to control inflammation and infection. The choice of treatment follows a stepwise approach and depends mainly on the severity, body sites involved, surface area affected and the patient’s age. (Table 1) Topical therapy is the mainstay of treatment for mild to moderate AE, and is also used in combination with oral therapy or phototherapy for severe cases. It includes adequate emollient use with properly titrated topical corticosteroids (TCs) and topical calcineurin inhibitors (TCIs). Topical antibiotics may also be considered for short-term usage depending on the presence of superimposed infection.

Emollients

The importance of emollients, or moisturizers, in the management of AE is often overlooked without realizing that stratum corneum abnormalities may be the primary exacerbating factors in AE. Apart from the reduction of scaling, roughness, and the sensations of tightness and itchiness, emollients also help to restore skin barrier function. Many different types of emollients are available, and they differ in their composition of active ingredients and excipients. Common topically applied lipids include petrolatum, beeswax, lanolin and triglycerides. They are often thicker in texture and exert their effects by forming an inert, epicutaneous protective membrane to reduce trans-epidermal water loss. However, recent research has shown that they may also diffuse more deeply into the skin. For example, petrolatum can be absorbed into the outer layer of delipidized stratum corneum. Besides these lipids, the inclusion of humectants (eg, urea, pyrrolidone carboxylic acid [PCA], lactic acid, glycerin, panthenol and sorbitol) in emollients further helps to maintain moisture in the stratum corneum, thereby increasing stratum corneum elasticity and reducing the risks of cracking and barrier

<table>
<thead>
<tr>
<th>Table 1. Stepwise management of atopic eczema</th>
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<tbody>
<tr>
<td>1. Generous emollient use (eg, barrier-repairing agents or occlusive agents) and soap avoidance</td>
</tr>
<tr>
<td>2. Mild to moderately potent topical corticosteroids +/- antimicrobial therapy +/- topical calcineurin inhibitors as maintenance or prophylaxis</td>
</tr>
<tr>
<td>3. High to ultra-high potency topical corticosteroids +/- antimicrobial therapy +/- topical calcineurin inhibitors as maintenance or prophylaxis</td>
</tr>
<tr>
<td>4. Wet-wrap therapy with topical corticosteroids</td>
</tr>
<tr>
<td>5. Phototherapy • NBUVB • PUVA • UVA1</td>
</tr>
<tr>
<td>6. Systemic agents or immunosuppressants • Corticosteroids • Antibiotics • Cyclosporine • Azathioprine • Mycophenolate mofetil • Intravenous immunoglobulin</td>
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</tbody>
</table>
disruption. Newer topical lipids, which are more ‘physiological’, can penetrate into the skin and modify endogenous epidermal lipids as well as the rate of barrier recovery. Emollients consisting of specific dermal lipids as well as the rate of barrier disruption. Newer topical lipids, which are more ‘physiological’, can penetrate into the skin and modify endogenous epidermal lipids as well as the rate of barrier recovery. Emollients consisting of specific ratios of cholesterol, fatty acids and ceramides have been shown to accelerate barrier recovery.\(^2\) Emerging evidence now indicates that these lipid mixtures and humectants may be more efficient than other ingredients in improving barrier function in AE, in addition to diminishing signs of dryness and pruritis. However, traditional topical lipids such as petrolatum still have an important role as they are cheaper and well tolerated even in infantile skin, with a lower risk of irritation and sensitivity.

Overall, the choice of emollients ultimately depends on the degree of moisturization required, the type of eczematous lesion, the body site involved, the cosmetic acceptability of the product to the patient, and the cost. Whichever type is chosen, it should be dispensed in an adequate amount and be applied regularly to maintain constant cutaneous hydration even if no actual inflammatory skin lesions are apparent clinically.

### Topical Corticosteroids

TCs, with their anti-inflammatory effects, have been for decades the mainstay in AE therapy for acute flare-ups and intermittent maintenance. They are available in different potencies and formulations. (Table 2) The appropriate choice depends on the severity of the AE, the body site involved, the age of the patient, and the patient’s response to previous TC treatment. Different therapeutic schemes have been established for its use, which include: 1) starting treatment with a more potent preparation to induce remission, followed by a relatively quick tapering down of preparation potency as the condition improves; 2) intermittent short bursts of a potent preparation followed by a steroid-free period of emollient use only until relapse occurs; or 3) more prolonged, continuous treatment with less potent preparations.\(^5,^4\)

Only mild to moderately potent preparations should be used on genital, facial or intertriginous skin areas for short-term applications. Furthermore, children should not be given high or ultra-high potency TCs. The basic principle is to use the least potent preparation that is effective for controlling the eczema.

The choice of an adequate vehicle, or base, is also important to achieve the optimal effect. Ointments rather than creams may be considered for more severe or lichenified lesions over thicker skin areas, such as palmoplantar lesions. Foam and lotion are more acceptable for hair-bearing sites, such as the scalp.

There is still no definite conclusion regarding the optimal frequency of application of the different types of TCs. A systemic review has shown that when clinical effectiveness and cost-effectiveness are considered, no clear difference in outcomes was seen between once-daily and more frequent applications of TCs.\(^3\) Patient education is important to maximize treatment efficacy, minimize side effects and increase compliance. Overall, TCs can be safely used if the above principles are observed. The well-reported adverse effects, listed in Table 3, are often due to the inappropriate use of preparations that are more potent than necessary, for prolonged periods over sensitive sites such as the face and intertriginous areas, especially in infants and children.

For children and adults with severe or refractory AE, short-term wet-wrap treatment (WWT) has been shown to be relatively safe and effective.\(^6,^7\) Wet-wrap treatment involves the application of a diluted TC ointment directly onto the eczematous areas, followed by a first layer of wet but wrung out gauze, and then a second layer of dry gauze on top. This treatment has the advantages of enhancing the penetration of TC, maintaining moisture and preventing scratching. Different regimens have been used for WWT, which include different types and concentrations of TCs, and application of the wet wrap at different frequencies for different durations. Although no large studies have been conducted to determine the optimal regimen, one example would be to use 10% dilution of a potent corticosteroid (eg, 0.1% mometasone furoate ointment) overnight for 12 hours per day for 7 days in cases of acute AE in children. Good long-term studies which evaluate systemic absorption and skin atrophy are still lacking. If there is overt impetiginization, WWT should be delayed. Common

<table>
<thead>
<tr>
<th>Potency</th>
<th>Class</th>
<th>Topical corticosteroid</th>
<th>Formulation</th>
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</thead>
</table>
| Ultra high | I | • Clobetasol propionate  
• Diflorasone diacetate | Ointment, 0.05%
Cream, 0.05% |
| High | II | • Betamethasone dipropionate  
• Flucinolone  
• Halcinonide | Ointment, 0.05%
Cream, 0.05%
Ointment, 0.1%|
| III | • Betamethasone dipropionate  
• Betamethasone valerate  
• Flucinolone propionate  
• Mometasone furoate  
• Triamcinolone acetonide | Cream, 0.05%
Cream, 0.1%
Ointment, 0.1%
Ointment, 0.0005%
Cream, 0.5% |
| Moderate | IV | • Flucinolone acetonide  
• Hydrocortisone valerate  
• Triamcinolone acetonide  
• Mometasone furoate | Ointment, 0.225%
Ointment, 0.2%
Cream, 0.1%
Cream, 0.1% |
| V | • Betamethasone valerate  
• Flucinolone acetonide  
• Hydrocortisone butyrate | Cream, 0.1%
Cream, 0.025%
Cream, 0.1% |
| Low | VI | • Desonide  
• Aclometasone dipropionate | Cream, 0.05%
Ointment, cream 0.05% |
| VII | • Hydrocortisone acetate  
• Methylprednisolone acetate | Cream, 1%
Cream, 0.25% |

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**Table 2. Topical corticosteroid potency chart**

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side effects of WWT include bacterial and viral skin infections, and chilling. Regular monitoring is therefore essential. Patient and parent education is also of fundamental importance to ensure compliance to therapy.

Topical Calcineurin Inhibitors

TCIs belong to a relatively new class of medication for the treatment of AE. They act by suppressing inflammatory cytokine production in activated T-cells and other inflammatory cells through the inhibition of calcineurin. Two topical formulations are currently available: 1) tacrolimus ointment (Protopic®) in two concentrations (0.1% for adults, 0.03% for children); and 2) 1% pimecrolimus cream (Eidel®). They can be applied twice daily, and have been proven to be as effective as moderately potent TCs with the advantages of very low systemic absorption and no steroid-associated side effects, such as skin atrophy, rebound and tachyphylaxis.

Numerous studies have proven the efficacy of TCIs for the treatment of acute phase AE, as well as for maintenance and as prophylaxis to prevent flares. Topical calcineurin inhibitors are particularly useful options for the treatment of sensitive sites, such as the face, periorbital, intertriginous and genital areas. For these anatomical areas, TCIs can be used at the first sign of flare-up to prevent disease progression. They are also valuable for patients who have already developed steroid-associated side effects. Another indication is as prophylaxis after control with TCs in the acute phase in patients with frequent flare-ups. TCIs are generally well tolerated with transient local irritation being the commonest side effect. They are contraindicated in skin with active infection, or in patients with weakened or compromised immune systems.

In 2005, the US Food and Drug Administration (FDA) issued a ‘black-box’ warning on TCIs regarding their associated potential cancer risk. This was based on information from animal studies of unusually high oral doses, which showed a subsequently increased risk of lymphoma. However, reviews of the malignancy cases reported in humans were unable to prove any causal relationship between the development of cancer and the use of TCIs. Even though the risk is of a theoretical concern, there is no evidence to date to suggest an increased risk of cutaneous or visceral cancer with topical use in the dosages employed clinically. The current FDA guideline recommends TCIs as a second-line short-term or an intermittent long-term treatment of AE in patients 2 years of age or older who are unresponsive to or intolerant of other conventional therapies. Continuous long-term application should be avoided as long-term safety is uncertain. Furthermore, a minimum amount of TCIs needed to control the patient’s symptoms should be used. Patients should be advised to minimize exposure of treatment sites to sunlight. As long as these guidelines are followed, TCIs continue to be a valuable option for optimizing long-term treatment in AE.

“Topical calcineurin inhibitors are particularly useful options for the treatment of sensitive sites”

Conclusion

The treatment of AE follows a stepwise approach. Emollients are often overlooked but are essential not only for the relief of dryness, but also for skin barrier protection and repair. TCs remain the most commonly used anti-inflammatory agent in AE. Selection of the appropriate potency, vehicle and duration of treatment would help to minimize their side effects. TCIs are useful alternatives for sensitive sites, and can also be used as maintenance or prophylaxis. Since their long-term safety is uncertain, they should only be prescribed for patients of 2 years of age or older and as an intermittent treatment.

Table 3. Side effects of topical corticosteroids

| Atrophic changes                  | • Steroid atrophy  
| Telangiectasia                    | • Steroid rosacea  
| Striae                           | • Hirsutism  
| Purpura                          | • Hyperpigmentation or hypopigmentation  
| Easy bruising                    | • Photosensitization  
| Ulceration                       | • Rebound flare of some dermatoses (eg, psoriasis) |

References

CLOBEX Shampoo: The proven power of clobetasol in a unique short-contact formulation

Comparative clinical efficacy to clobetasol leave-on gel therapy in moderate to severe scalp psoriasis

In clinical trials, CLOBEX Shampoo was not associated with telangiectasia or skin atrophy

References:
1. Roepcke P et al. A new shampoo formulation of clobetasol propionate 0.05% is at least as efficacious and safe as clobetasol propionate gel 0.05% in the treatment of scalp psoriasis. Poster presented at EADV 2000.
5. Appel P et al. A new formulation of clobetasol propionate 0.05% is more effective and safer than 1% tar shampoo in scalp psoriasis. Poster presented at EADV 2002 and AAD 2000.

Change in Skin Thickness From Baseline to the End of Treatment (week 4) vs. Clobetasol Propionate Gel 0.05%

Further information available on request from Galderma Hong Kong Ltd. Tel +852 2824 0333
Unit 1401, 14/F, Ming An Plaza, Phase 1, 8 Sunning Road, Causeway Bay, Hong Kong.
The skin is the largest organ in the body and is most accessible for clinical assessment. There are frequent associations of skin signs with internal diseases. (Table 1) In a survey of inpatient dermatological referrals, 48% of skin lesions were found to be related to the presenting illness, in which 36.6% of skin conditions contributed to the diagnosis of systemic disease. Important and sometimes subtle skin signs of systemic diseases should not be overlooked. Clues to underlying systemic conditions can be obtained by careful skin examination that can lead to early diagnosis.

<table>
<thead>
<tr>
<th>Table 1. Skin signs of systemic disease</th>
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<tbody>
<tr>
<td><strong>Infections</strong></td>
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<tr>
<td>Syphilis</td>
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<tr>
<td>Tuberculide</td>
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<tr>
<td>Meningococcaemia</td>
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<tr>
<td>Infective endocarditis</td>
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<tr>
<td>Scrub typhus</td>
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<tr>
<td>Typhoid rose spots</td>
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<tr>
<td>Staphylococcal scalded skin syndrome</td>
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<tr>
<td>Disseminated gonococcal infection</td>
</tr>
<tr>
<td><strong>Paraneoplastic</strong></td>
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<tr>
<td>Tylosis</td>
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<tr>
<td>Leukemia cutis</td>
</tr>
<tr>
<td>Pruritus</td>
</tr>
<tr>
<td>Carcinoid</td>
</tr>
<tr>
<td>Sweet’s syndrome</td>
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<tr>
<td>Dermatomyositis</td>
</tr>
<tr>
<td>Tripe palms</td>
</tr>
<tr>
<td>Paraneoplastic pemphigus</td>
</tr>
<tr>
<td>Glucagonama</td>
</tr>
<tr>
<td>Pyoderma gangrenosum</td>
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<tr>
<td><strong>Hypersensitivity</strong></td>
</tr>
<tr>
<td>Henoch Scholein purpura</td>
</tr>
<tr>
<td>Erythema nodosum</td>
</tr>
<tr>
<td>Serum sickness</td>
</tr>
<tr>
<td>Erythema multiforme</td>
</tr>
</tbody>
</table>

| **Rheumatological**                   |
| SLE                                   |
| MCTD                                  |
| Scleroderma                           |
| Psoriatic arthropathy                 |
| Bechet’s disease                      |
| Dermatomyositis                       |
| Adult Still’s disease                 |
| **Endocrine / Metabolic**             |
| Diabetic sclerodema                   |
| Pretibial myxedema                    |
| Necrobiosis lipiodica                 |
| Acanthosis nigricans                  |
| Xanthoma                              |
| Pancreatic panniculitis               |
| Porphyrias                            |
| **Genetic disease**                   |
| Neurofibromatosis                     |
| Pseudoxanthoma elasticum              |
| Tuberous sclerosis                    |
| Hereditary haemorrhagic telangiectasia|

SLE = systemic lupus erythematosus; MCTD = mixed connective tissue disease

**Paraneoplastic Dermatoses**

A number of skin disorders have been linked to internal malignancy. The cutaneous features can sometimes precede the manifestation of underlying malignancy for months, providing an opportunity for diagnosis at early stages. Carcinoma of the oesophagus has been associated with palmpplanter hyperkeratosis (tylosis). Carcinoma of the gut, lung and breast may present with acanthosis nigricans and tripe palms, which is considered a form of palmar acanthosis.
nigricans with corrugated thickening of the palms. Patients with metastatic carcinoma tumour have episodes of flushing of the face, neck, and sometimes the trunk. Dermatomyositis is most commonly associated with nasopharyngeal carcinoma, as well as carcinoma of the lung, colon and breast. (Figure 1) Superficial migratory thrombophlebitis (Trousseau’s sign) is most likely to be associated with carcinoma of the pancreas. Glucagonoma produces necrotic migratory erythema with dusky red, annular and scaly papulopustules on the trunk. Cutaneous features associated with haematological malignancy include Sweet’s acute febrile neutrophilic dermatosis, pyoderma gangrenosum, leukaemia cutis, cutaneous lymphoma, paraneoplastic pemphigus and erythroderma in Sézary syndrome.

**Generalized Pruritus and Systemic Disease**

Pruritus is itching that leads to scratching in the absence of visible lesions. Obstructive jaundice causes severe pruritus. It is especially an early feature of primary biliary cirrhosis, and bile salts rather than bilirubin are responsible for the itch. Iron deficiency has also been linked to itching even before patients are anaemic. Polycythaemia is frequently associated with itching, particularly after a hot bath. Pruritus occurs in 25% of patients with Hodgkin’s disease, often associated with ichthyosis.

Patients with chronic renal failure often suffer greatly from pruritus that cannot be relieved by dialysis. Parathyroidectomy may relieve itching in patients who require removal of the gland due to secondary hyperparathyroidism. The cause of pruritus in renal failure is unknown, but raised histamine levels, endogenous opioids, and dryness of the skin are contributing factors. Mast cell numbers are also increased in uremic patients. Pruritus is sometimes a presenting symptom of diabetes mellitus, but this is principally localized to the genitalia because of candidiasis. Ten percent of patients with hyperthyroidism complain of itching, and dry skin in hyperthyroidism often itches. Drugs that can induce pruritus including opiates, and those causing cholestasis or inducing subclinical hypersensitivity.

**Rheumatological Disease and Skin**

When psoriatic lesions are accompanied by arthritis, the possibility of psoriatic arthritis or Reiter’s disease should be considered. A history of uveitis and/or urethritis points to the latter diagnosis. In scleroderma, there are mat telangiectasias that are telangiectatic macules measuring 2 to 7 mm in diameter commonly found on the face, oral mucosa and hands. Mat telangiectasias are also an important clue to the diagnosis of the CREST (calcinosis cutis, Raynaud’s phenomenon, oesophageal dysmotility, sclerodactyly, and telangiectasia) syndrome, as they may be the only cutaneous finding. Periungual telangiectasias are pathognomonic signs of lupus erythematosus, scleroderma and dermatomyositis. In dermatomyositis, the erythema is often accompanied by “ragged” cuticles.

**Infections and Skin**

In secondary syphilis, there are scattered reddish-brown papules with thin scales. The eruption often involves the palms and soles, and can resemble pityriasis rosea. Nonscarring alopecia, condyloma lata and mucous patches as well as lymphadenopathy, malaise, fever, headache and myalgia are associated findings that are helpful for making the diagnosis. The interval between the primary chancre and the secondary stage is usually 4 to 8 weeks.

The embolic lesions in acute meningococcal sepsis are found mainly on the trunk and lower extremities. Associated findings include a preceding upper respiratory tract infection, fever, meningitis and disseminated intravascular coagulation. In disseminated gonococcal infection, a small number of papules and pustules with central purpura or haemorrhagic necrosis are found on the distal extremities. Additional symptoms include arthralgia, tenosynovitis and fever. Scrub typhus is a rickettsial infection characterized by high fever and light pink eruptions 2 to 5 mm in diameter on the trunk and extremities. With time, the lesions can become purpuric. Careful search may reveal an eschar that corresponds to the bite of a mite.

**Panniculitis or Vasculitis as Nodular Rashes**

Inflammation of adipose tissue presents as subcutaneous nodules and is frequently a sign of systemic disease. There are several forms of panniculitis, including erythema nodosum, erythema induratum/nodular vasculitis, lupus profundus and fat necrosis secondary to pancreatic disease. Histological examination of deep incisional biopsy specimens will aid in the diagnosis of the particular type of panniculitis. Except for erythema nodosum, these lesions may break down and ulcerate or heal with a scar. Nodules of erythema nodosum are most commonly found on the shin, whereas lesions of erythema induratum are most commonly found on the calf. In erythema nodosum, the nodules are initially red but eventually become bruise-like lesions as they resolve. Patients may have fever, malaise, leukocytosis, arthralgia and/or arthritis. The possibility of an underlying illness should be excluded, and the most...
common associations are tuberculosis, streptococcal infections and inflammatory bowel disease in addition to drugs (oral contraceptives, sulfonamides). Erythema induratum is associated with the presence of Mycobacterium tuberculosis DNA by PCR assays of skin lesions.

The lesions of lupus profundus are found primarily on the upper arms and buttocks, and are seen in both the cutaneous and systemic forms of lupus. The overlying skin may be normal or erythematous, and localized fat atrophy may eventually occur. Subcutaneous fat necrosis that is associated with pancreatic disease is presumably secondary to circulating lipases, and is seen in patients with pancreatic carcinoma as well as in patients with acute and chronic pancreatitis.

Subcutaneous erythematous nodules are also seen in medium-sized vessel vasculitis such as polyarteritis nodosa (PAN), Churg-Strauss syndrome or Wegener’s granulomatosis. Cutaneous PAN presents with painful subcutaneous nodules and ulcers within livedo reticularis. In both the cutaneous and systemic forms of vasculitis, skin biopsy specimens of the associated nodules will show fibrinoid necrosis characterizing vasculitis.

**Endocrine Disease and Skin**

There are a number of cutaneous changes in diabetes mellitus. Diabetic dermopathy produces hyperpigmented dull-red papules with superficial scales on the shins. It heals with atrophic brown scars. Diabetic thick skin may be localized to the neck and upper back (sclerodermia of Buschke) or the dorsum of the hands (cheirarthropathy). Acanthosis nigricans is common in obese insulin-resistant diabetic patients, while generalized granuloma annulare, diabetic bullae, lipoatrophy and perforating disorders are less common. Necrobiosis lipoidica diabetorum (NLD) is a characteristic eruption of yellowish waxy plaques on the shin, which eventually become atrophic in the centre and may ulcerate. (Figure 2) NLD occurs in 0.3% of diabetic patients and may predate diabetes. Hyperlipidaemia in diabetic patients may be associated with xanthoma.

**Intestinal Diseases and Skin**

Major aphthous ulcers are a feature of Bechet’s syndrome, while minor aphthae are found in systemic lupus erythematosus, Crohn’s disease, as well as iron deficiency. Gastric polyposis is associated with perioral lentigines in the Peutz-Jeghers syndrome. Erythema nodosum, oral aphthous ulcers and pyoderma gangrenosum are also associated with inflammatory bowel disease, along with the secondary skin changes due to malabsorption. (Figure 3) The stigmata of chronic liver disease include spider naevi, palmar erythema, purpura, leukonychia and clubbing of the fingers. There is also loss of pubic hair. Gynaeomastia, xanthoma, jaundice, pruritus and pigmentation are other features. Porphyria cutanea tarda, haemochromatosis and primary biliary cirrhosis produce diffuse skin pigmentation.

**Evaluation of Patients With Significant Rashes**

Most patients who present with a rash have no systemic disease, but patients can sometimes present with cutaneous manifestations of internal diseases. In parallel with necessary investigation, simple empirical treatment of the skin with emollients and appropriate topical medications may already result in resolution of rashes. The sudden onset of persistent rashes in an otherwise healthy, normal individual warrants further work-up, including thorough history taking and physical examination as well as laboratory studies, such as complete blood count, erythrocyte sedimentation rate, serum biochemistry, thyroid function, autoimmune markers, chest radiograph and skin biopsy. Extensive imaging and endoscopic studies are reserved for those with suggestive clinical evidence and positive findings in initial work-up. Follow-up assessment of patients with unexplained eruptions is important in order to detect emerging features of systemic diseases.

**References:**

We are pleased to announce the ninth in our series of multidisciplinary CME-accredited meetings, which will be held on Saturday, 10 October 2009. The programme for the meeting is as follows:

12:30 – 1:50 pm  Registration and buffet lunch
1:50 – 2:00 pm  Opening remarks
2:00 – 2:45 pm  From evidence to action: Towards lower LDL-C target
Dr Norman Chan
Specialist in Endocrinology, Clinical Director, Qualigenics Diabetes Centre, Hong Kong
2:45 – 3:15 pm  Updates on paediatric pneumococcal diseases
Dr Yat-Wah Kwan
Associate Consultant, Department of Paediatrics and Adolescent Medicine, Princess Margaret Hospital, Hong Kong
3:15 – 3:30 pm  New frontiers in pneumococcal prophylaxis
Dr Frank Fan
Medical Director, Wyeth Hong Kong
3:30 – 3:50 pm  Coffee break
3:50 – 4:35 pm  Clinical approach to alopecia in general practice
Dr Tze-Yuen Lee
Specialist in Dermatology and Venereology, Hong Kong
4:35 – 4:55 pm  Case sharing: Medico-legal issues in primary care practice
Dr Stephen K S Foo
Specialist in Family Medicine; Member, Preliminary Investigation Committee, Medical Council, Hong Kong
4:55 – 5:00 pm  Closing remarks

The Primary Care Clinic aims to deliver a rewarding CME experience. Delegates joining this meeting will be accredited Continuing Medical Education (CME) points. Applications to the respective academic institutions and committees have been submitted and approval is pending. CME points to be awarded by the various colleges/societies will be updated on our Website soon.

Registration Form
Saturday, 10 October 2009 (12:30 – 5:00 pm)

Online registration: www.theprimarycareclinic.com

Personal Information
Title:  ○ Prof  ○ Dr  ○ Mr  ○ Mrs  ○ Miss  ○ Ms
Surname: ______________________  Given Name: ______________________
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Please complete the registration form (or a photocopy of the form) with payment and return to:
CMPMedica Pacific Ltd., 9/F, CNT Tower, 338 Hennessy Road, Wan Chai, Hong Kong. (Attn.: The Primary Care Clinic). Credit card payments are acceptable via fax (852) 2559 6910.
For enquires, please call (852) 2116 4340 or e-mail cme@asia.cmpmedica.com

Terms and conditions: 1. All payments must be made in Hong Kong Dollars. 2. Payment is non-refundable. 3. Registration form with payment must reach CMPMedica 2 weeks before the event. 4. Seats are confirmed only if you receive a confirmation letter from CMPMedica. 5. Certificate of attendance will be awarded upon completion of the course.

HK$150 per person
Free registration will be offered to members of The Society of Physicians of Hong Kong on a first come first served basis.

The Society of Physicians of Hong Kong

Date: Saturday, 10 October 2009
Location: The Langham Hong Kong
8 Peking Road, Tsimshatsui, Kowloon
Time: 12:30 – 5:00 pm
When soap is a dirty word

is the gentlest soap-free cleanser\(^1\) for dry sensitive skin.

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For dry sensitive skin, use Cetaphil Gentle Skin Cleanser. It is gentler than soap and other soap substitutes.\(^1\)