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Update on Therapeutics in Dermatology

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Editor



Dr. LY Chong

Just like the other branches in modern medicine, dermatology has been developing rapidly in the developed countries. However, these developments may not be aware by non-dermatologists or in under-developed areas where the major health resources still have to be allocated solely to life-threatening conditions. It is therefore necessary to update these changes from time to time to keep pace with modern medicine. In this issue, the theme is mainly focused on the therapeutics in dermatology, from the very basic principles to the recent advances.

In the article of "Proper use of topical corticosteroids and topical immuno-suppressive agents" by Dr. K.K. Lo, the author has given an overall review on topical corticosteroid, a mainstay therapeutic option for inflammatory dermatoses that almost every clinician will prescribe. Misuse of these agents is however still very common, even in a developed area like Hong Kong where the standard of medical care is considered high. As a result, patients with steroid-induced atrophy and striae are commonly seen. Adrenal suppression, Cushing syndrome and growth retardation in children have been encountered from time to time. These have caused significant morbidity in patients and sometimes aroused medico-legal disputes. Besides topical steroid, the recent hot topic in the media about the potential side-effects of topical immuno-modulators has also been discussed in this article.

Even with good therapeutic efficacy, a topical agent needs good absorption and good compliance of the patients to achieve its effect. In the article of "Proper choice of base of topical medicaments" by Dr. K.M. Ho, the principles of choosing a proper base of a topical agent have been reiterated. The proper choice of a base has often been neglected by the doctor who prescribes the topical agent, not aware that this will affect the overall success rate in the treatment.

In the Drug Review column, Dr. K.H. Lau has focused on the recent pharmaceutical breakthrough in treating psoriasis. Though still unable to cure psoriasis, biologics do present a new treatment option in this disease. Various different biologics are now available in the market and different pharmaceutical companies have aggressively promoted the merits of their own drugs. As a result, clinicians may be confused in choosing the appropriate biologic for their psoriatic patients. In the article of "Comparison of various biological agents in the treatment of psoriasis", the author has compared various different biologics for reader's reference. Behind the enthusiasm with this group of drugs, there are also worries with regard to their potential side-effects, such as serious infections and immunoproliferative neoplasms. These are issues that clinicians have to consider when using these biologics.

Besides the pharmaceutical agents, other armamentaria in dermatology have been discussed in the article of "Practical Office-based Dermatological Procedures" by Dr. W.Y.M. Tang. These are practical and pragmatic procedures that can be readily carried out in



the clinics of dermatologists or general practitioners with proper training. It greatly enhances our skills in treating various dermatological diseases that may not be satisfactorily dealt with by pharmacological means.

In the Abstracts column, Dr. H.T. Yu and Dr. M.C. Wong have reported on photodynamic therapy and botulinum injection presented in the 2006 Annual Meeting of the American Academy of Dermatology. Both are state-of-the-art therapeutic measures in dermatology. Aesthetic dermatology is a rapidly developing branch in dermatology as beauty loving is human nature, and there is no reason why it cannot live in symbiosis with medical dermatology. In fact, it has substantially broadened

the boundary of this specialty.

Last but not least is a very interesting and soft article from Dr. H.C. Fung, a keen and good violin player. In his article of "Medicine and Music", he has lively linked up these two arts that have tremendous impact on human beings. This article actually serves as a delicious dessert in this issue after all these "orthodox" scientific papers ahead. To improve our quality of life, there are many more things we can enjoy apart from career, fame and wealth. Music can soften our heart and relieve our tension after a day's hard work. I am sure some readers may be keener to read this article than the scientific papers.



Proper Use of Topical Corticosteroids and Topical Immuno-suppressive Agents

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Dr. KK Lo

Topical hydrocortisone was first successfully used in the treatment of skin dermatoses by Sulzberger and Witten in 1952¹. The prescription of topical corticosteroids marked the most important milestone in the history of dermatological treatment. The problem with topical corticosteroid is that the same mechanisms of action responsible for their therapeutic effects (anti-inflammatory and anti-proliferative effects) can also lead to adverse effects. The ideal skin-selective corticosteroid has yet been difficult to develop because the intracellular receptors that are responsible for corticosteroid efficacy are also responsible for manifestations of the adverse events².

The anti-inflammatory effects of topical steroids are quite complex. The corticosteroid molecule binds to specific cytoplasmic steroid receptors of the keratinocytes and other cells in skin. It is transported to the cell nucleus, where it interacts with high-affinity binding sites on nuclear DNA. Steroid induced proteins, called lipocortins, are then synthesised by the target cells. These proteins then inhibit phospholipase A2, an enzyme necessary for arachidonic acid formation. This results in the decrease of the formation of several potent inflammatory mediators, including prostaglandins, leukotrienes, and platelet activating factor. Subsequently, polymorphonuclear leukocytes show decreased migration, phagocytosis, adherence, and numbers at sites of inflammation. Monocytes, lymphocytes, and Langerhans cells also show decreased function and numbers at sites of inflammation. These proteins have also been shown to decrease vascular permeability and to produce vasoconstriction, thus decreasing tissue oedema, erythema and heat.

The most important aspect for a clinician to remember in prescription of topical corticosteroids is to prescribe for the appropriate dermatoses³ (Table 1). There are different strengths of topical steroids (Table 2) that are used to treat different phases of the disease and also for the disease at different anatomical locations. In general, mild corticosteroids can be safely given to treat acute inflammatory skin lesions of the face and flexural areas whereas moderately potent ones are often required to treat chronic, hyperkeratotic or lichenified lesions on palms or soles. Most preparations are advised to apply once or twice daily though more frequent applications to the palms and soles may be warranted as the topical corticosteroids are difficult to be absorbed and easily removed during normal activities. For chronic stable lesions, every-other-day in lichen simplex chronicus or weekly applications may offer the same therapeutic effect as daily application e.g. in treatment of vulval

lichen sclerosis et atrophicus. For those patients psychologically requiring something to apply daily, the prescription of bland emollient cream may help. Fetal abnormalities due to topical corticosteroids have not been documented in human beings but it is still recommended that it should be restricted to times when the potential benefits justify the potential risk to the foetus as there were foetal abnormality data in animal studies when using a large amount in occlusive dressing⁴.

The vehicle of topical corticosteroids also plays some important role for their efficacy and absorption (Table 3). Ointment though more greasy and difficult to spread are preferred for chronic lichenified lesions as they enhance penetration by means of their occlusive effect. Creams or lotions are preferred for acute and subacute dermatoses and used on moist skin or flexural areas. Absorption of topical corticosteroids varies from region to region⁵ (Table 4). For example, penetration varies between the eyelids and the sole by nearly 300 fold. It should be noted that these data were obtained from normal healthy skin. In atopic dermatitis there is a defective epidermal barrier and the penetration of topical corticosteroids can be two to ten folds higher than that of normal healthy skin. In the flexural area, there will be the additional physical effect of occlusion by skin folds that will also enhance absorption. For these reasons, the use of topical corticosteroids in these areas: scrotum, face especially eyelids, flexures should be extremely cautious and closely monitored. It is especially true in the very young and the very old. The safest is to use the least potent topical corticosteroid (i.e. hydrocortisone acetate 1% cream) in a limited period with intermittent application of emollients to reduce the frequency of application. It has been documented that emollient adjunctive therapy offers a steroid-sparing effect in the treatment of atopic dermatitis⁶.

Even for skin of other areas, the close supervision of the use of topical corticosteroids and monitoring of the response of the skin diseases will be essential in reducing the unwanted adverse effects of topical steroids² (Table 5). With clear instructions and good patient education by the clinician, the fears on topical corticosteroids can be dispelled. For many patients, the proper intermittent use of topical corticosteroids is still highly effective and the benefits definitely outweigh the risk.

The non-steroid topical immunosuppressive agents available over the market in recent years have generated great excitement and hopes to both clinicians and their patients. Topical tacrolimus and topical pimecrolimus are the two available products that are indicated to treat atopic dermatitis. These products do not cause skin



atrophy as they do not alter the collagen synthesis. The commonest adverse reactions are mild skin burning and pruritus. Others like headache, allergic reaction, skin infection, acne and folliculitis have been reported. It is now not recommended to give it to children less than two years old and should not be used with occlusive dressing. Long term use is not clearly defined and short term and intermittent usage are acceptable but should be recommended as second line of therapy for atopic dermatitis. The carcinogenesis associated with the long term use of these topical immuno-suppressants in animal models is something of concern⁷. These compounds definitely have a role in the management of atopic dermatitis in certain sites e.g. facial lesions especially those around the eyes where topical corticosteroids are most concerned of their adverse effects.

In conclusion, topical corticosteroids having more than 50 years of treatment records in skin therapy bear minimal risk provided that they are correctly prescribed for the right dermatoses and constantly supervised by medical practitioners. The principles of optimal use of topical corticosteroids are as follows: to prescribe for the appropriate dermatoses; to use appropriate potency and strength of topical corticosteroids to achieve disease control; to either continue with a less potent preparation or reduction of frequency of application after sufficient clinical response; to taper off the treatment upon complete remission of skin diseases; to pay special attention and caution when prescribing topical steroid to certain locations (e.g. scrotum, face, flexures and peri-orbital regions) and when prescribing to the elderly and children. The use of topical immuno-suppressive macrolides, tacrolimus and pimecrolimus should be used with caution on long term basis. All doctors prescribing these compounds should be aware of the potential consequences of long-term topical immunosuppression. The long term safety profile of these topical immunosuppressive compounds warrants more evaluation in future though the short term use and intermittent use of these compounds have passed all the safety regulations and requirements of health authorities in most countries.

Table 1 Indications for use of topical corticosteroids³

Indications	
Various types of dermatitis and eczema	Atopic dermatitis, lichen simplex chronicus, prurigo, seborrhoeic dermatitis, nummular eczema, housewife dermatitis, allergic contact dermatitis, Pompholyx,
Psoriasis	Chronic plaque type, localized pustular type, inverse psoriasis
Autoimmune bullous dermatoses	Bullous pemphigoid, pemphigus foliaceus, cicatricial pemphigoid
Connective tissue diseases	Lupus erythematosus, dermatomyositis, morphea
Others	Lichen sclerosis et atrophicus, lichen planus, alopecia areata, vitiligo, keloid, pyoderma gangrenosum, Behcet's disease, granuloma annulare, insect bite reactions, early stage of cutaneous T-cell lymphoma, polymorphous eruption of pregnancy, Well's syndrome.

Table 2 Class of topical corticosteroid preparations

Group	Class	Example
Very potent	Class 1	Clobetasol propionate ointment & cream 0.05%, halobetasol propionate ointment 0.05%, betamethasone dipropionate ointment & cream 0.05%
	Class 2	Fluocinonide 0.05% ointment, mometasone furoate ointment 0.1%, triamcinolone acetonide ointment, 0.5%, halcinonide cream 0.1%
Moderately Potent	Class 3	Betamethasone valerate ointment 0.01%, fluticasone propionate ointment 0.005%, flucortolone cream 0.5%
	Class 4	Betamethasone valerate 0.01% lotion, fluocinolone acetonide cream, 0.025%, hydrocortisone valerate ointment 0.2%, mometasone furoate cream 0.1%, hydrocortisone butyrate cream and ointment 0.1%
	Class 5	Betamethasone dipropionate lotion 0.05%, betamethasone valerate cream 0.01%, fluocinolone acetonide cream, 0.025%, fluticasone propionate cream 0.05%, hydrocortisone valerate cream 0.2%
Mild	Class 6	Fluocinolone acetonide cream 0.005%, triamcinolone acetonide cream 0.02%, aclometasone dipropionate cream 0.05%, desonide cream 0.05%
	Class 7	Hydrocortisone acetate cream 1%

Table 3 Choosing a preparation: Vehicle for topical steroid

Preparation	composition	Moisturizing effect	Preferred site	Potential for irritation
ointment	Water in oil	Very moisturizing - greasy	Thick, lichenified skin, palm & soles	Low
Cream	Oil in water emulsion	Moderate in moisturizing - cosmetically elegant	Acute, subacute or weeping dermatoses, for moist skin	Variable; required preservatives
Gel	Cellulose with alcohol or acetone	Drying	Scalp	High
Lotion	Oil in water	Drying	Scalp	High

Table 4 Regional variation in the percutaneous absorption in normal skin of hydrocortisone in man⁵

Anatomical location	% of hydrocortisone absorbed
Sole	0.14
Ankle	0.42
Palm	0.83
Forearm	1.1
Back	1.7
Scalp	3.5
Axilla	3.6
Forehead	6
Jaw angle	13
Scrotum and eyelids	42

Table 5 Adverse effects of topical corticosteroids

Categories	
Atrophic changes	Steroid atrophy, telangiectasia, striae, purpura, ulceration, easy bruising
Infections	Mask fungal infection (tinea incognito), worsening of cutaneous infections: herpes, demodex, candidiasis, granuloma gluteale infantum
Ocular changes	Glaucoma, cataract
Pharmacologic effects	Steroid rebound, steroid addiction, tachyphylaxis
Others	Steroid acne, perioral dermatitis, steroid rosacea, hirsutism, hyperpigmentation, hypopigmentation, photosensitization, contact allergic dermatitis; adverse effects due to systemic absorption

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Proper Choice of Base of Topical Medicaments

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Dr. KM Ho

Introduction

All topical drugs have to pass through the outermost layer of the skin before they can exert their pharmacologic effects. The stratum corneum of the epidermis is constructed like the "bricks and mortar" of a brick wall. The lipid substance originated from the keratinocytes constitutes the mortar of this biological wall. This natural barrier not only helps to prevent water from losing from the body but also exogenous substances from getting into the body. It is therefore easily envisaged that lipid soluble substances can pass through the stratum corneum better than the water soluble one. For the non-lipid soluble substance, alternative pathways such as transcellular transport, or diffusion through the sebaceous ducts, hair follicles or sweat ducts may be required for action. These substances can however be delivered by lipid carriers, the base, to the skin. The host factors may affect the bioavailability of the topical medicaments. Disrupted epidermis such as active eczematous state, better hydrated skin and skin under occlusion facilitates local absorption. Thinner skin as of the scrotum, face and neonates absorb local medicaments more efficiently as compared to the palms, soles, and normal adults respectively.

Many of the dictums in dermatologic therapeutics are established before the era of "evidence-based medicine". This review article attempts to briefly outline the general principles of topical therapeutics from the perspective of a dermatologist in practice.

Choosing the preparation

The Polano triangle summarizes the composition of the vehicle (base) of various traditional topical formulations. Briefly, these are powder, grease, liquid, or combinations of any two (or three) of them. Examples are: ointment is pure grease, vanishing cream is "water in oil", lotion or solution is purely liquid, shake lotion is "powder in liquid" and paste is "powder in grease" preparation. The pharmaceutical companies may sometimes use the terms more from the perspective of the consumers. Therefore doctors are strongly advised to read the product inserts for exactly what are the components and base of the topical drugs prescribed (see examples below).

Cream

Depending on the proportion of water to grease, cream

can be water miscible and washed away easily or be thick and sticky. It is perhaps the commonest prescribed topical medicament. As it is less oily, messy and sticky, most patients find it more user-friendly as compared to ointment. Because of its water content, some patients may find it soothing as a result of water evaporated from the applied area, and therefore the classic teaching says that it is more suitable in acute weeping lesions. Nevertheless, also because of its water content, preservatives have to be added and as a result, it may lead to a higher risk of allergic contact dermatitis as compared to ointment. For the same token, some patients may find it irritating when it is applied to raw or "hyper-acute" lesions. It is understandable; the readers can imagine the feeling of running water to their newly injured wound. There are also patients especially ladies who have what they describe as "sensitive" skin, find themselves difficult to tolerate many cream preparations.

Creams can be prepared by varying the proportion of water and grease. The standard aqueous cream is composed of about 70% water and 30% grease. Generally speaking, the higher the proportion of grease in the cream base, the more "oily" or "thick" the cream will be. This will affect the efficacy of the formulation if the cream is designed to be used as moisturizing cream. Although "thinner" preparation is more welcome by patients, they may be required to reapply the moisturizing cream more frequently in order to keep their skin hydrated and succulent. To illustrate, Oilatum Cream™ of Stiefel contains about 20% grease while Oilatum Plus™ of Stiefel contains more than 50% grease.

Storage of cream preparation may be more demanding as too warm and humid environment may facilitate the growth of environmental bacteria and fungi while too dry may desiccate the cream. Instruction for storage is not an uncommon oversight in the busy practice of doctors.

Ointment

These are formulations normally composed of greases, usually anhydrous, in semi-solid phase. The greases may be a combination of soft or liquid paraffin or lanolin or others. These preparations may be preservative free. They are more occlusive and hence preserve water in skin better as compared to cream. The classic teaching says that ointments are the better preparations for chronic and dry lesions. Most local patients do not however like ointment because of the greasiness



especially when it is required to be applied to the face, hairy areas, intertriginous areas, the palm and soles. Greasy preparations may however be used in the hairy areas to remove the greasy scales as in e.g. seborrhoeic dermatitis of the scalp of the newborn and psoriasis of scalp. Ointment is the only available preparation for some topical medicaments e.g. tacrolimus, mupirocin, Whitfield.

Gel

These are clear jelly like semisolid formulations composed of high molecular polymers (e.g. cetomacrogol) in an aqueous or alcoholic base. They are drying and hence cooling and not greasy. They are more suited for applying on greasy or hairy areas of the body such as the face and scalp. Because of their drying effect and perhaps also alcoholic component, they may cause irritation especially in those acute lesions. Fluocinolone acetonide has the gel formulation that is not uncommonly prescribed to treat scalp psoriasis. Clindamycin has the gel formulation to treat facial acne. Topical retinoid in cream base is better tolerated as compared to gel base formulation of the same concentration.

Lotion

Lotion is liquid formulation mostly composed of drugs dissolve or dispersed in an aqueous base. While some pharmaceutical companies reserve the term solution for liquid formulations that contain alcohols, the author suggests that doctors should refer to the package insert for detail description if the particular formulation contains alcohol or not. It is more user-friendly when the topical medicament is to be applied to a large area of the body or to hairy areas. Because the water/alcohol content within the lotion formulation is more easily evaporated, it will give a cooling sensation to the skin. An example is calamine lotion, a shake lotion (solid in water), that is commonly used for relieving the irritation of miliaria in children by making use of its cooling and hence soothing effect. As for the other aqueous preparations or those containing alcohol, it may cause irritation to raw areas or acute lesions and aggravate dryness of the skin. Occasionally, grease in water formulations may also use the term lotion. These are usually skin care products in

which the grease portion may only compose of less than 10-20% in the formulation e.g. 5% white soft paraffin in QV Skin Lotion™ of Ego.

Other preparations

There are also antifungals in powder formulations in the market. The advantage may be that it can absorb excessive sweating in areas such as the soles and does not have the slippery sensation when applied to the soles. Paste is solid in grease formulation. Tar paste is the classic example in this category. It has fallen out of fashion in recent years. Topical steroids and antifungals have also been prepared in spray formulations either locally or in other countries. Foam vehicles have also been developed to carry topical steroids in the US.

In-house mixing of your own formulation is generally not recommended. The ingredients and occasional bases may not be compatible with each other. There are also risks of contamination and non-homogenous mixing.

Other important ingredients within the base

Some formulations contain propylene glycol that enhances the bioavailability of the active ingredients e.g. Diprocel Cream™ Schering-Plough is more potent than Diprosone Cream™ Schering-Plough although both of them contain 0.05% betamethasone dipropionate. Because of the presence of propylene glycol in the former, it may sometimes lead to contact dermatitis either irritant or allergic. Lanolin that is in fact a group of heterogeneous fatty substances may be present in the cream/ointment base. Some patients may have allergic contact dermatitis to some of these substances.

Summary

Proper drug and formulation should be chosen according to the disease severity, sites involved and the personal profile of the host. Remember there are two components, the drug and the base in the topical formulations and we have to know what they are in order to maximize the therapeutic benefits.



Practical Office-based Dermatological Procedures

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The modern era of dermatological practice is dominated by laser and light related procedures. There are however, other procedures that can be carried out in a dermatologist's surgery to effect diagnosis and treatment. This paper will review some of these procedures (Table 1) which have been performed by the author or his colleagues.

Table 1: Some office-based dermatological procedures

Procedure	Indication/s
Cryosurgery	Viral wart, seborrhoeic keratosis, skin tag, haemangioma, molluscum contagiosum, porokeratosis, lentigo, actinic keratosis, basal cell carcinoma etc.
Phototherapy: Broad band UVB, narrowband UVB, PUVA	Psoriasis, eczema, vitiligo, lichen planus, alopecia areata, urticaria pigmentosa etc.
Diluted steroid wet wrap treatment	Atopic dermatitis
Electrotherapy: Iontophoresis	Primary focal hyperhidrosis Palmoplantar eczema exacerbated by sweating
Electrotherapy: Transcutaneous electrical nerve stimulation (TENS)	Postherpetic neuralgia Pruritus
Skin biopsy: incisional, excisional, punch, shave	For diagnosis and/or treatment of skin diseases
Skin flap surgery	Excision of large skin tumour
Nail: Tube insertion	Splinting of uncomplicated ingrowing toenail

Cryosurgery

Cryosurgery is useful for treating a wide array of benign and malignant conditions (Table 1).¹ It destroys diseased tissue by extreme cold in a controlled manner. The cryogen (liquid nitrogen, carbon dioxide and nitrous oxide etc.) can be delivered via a 'cryojet' gun, probe, a cone, a dipstick or a pair of forceps to the target tissue. Each freeze-thaw cycle lasts for seconds, causing intracellular ice formation leading to tissue cell necrosis, vascular stasis and deranged microcirculation. Among the cryogens, liquid nitrogen has the lowest boiling point at -196°C and thus is effective for treating premalignant and malignant lesions. Cryosurgery does not usually require anaesthesia and is suitable for most patients of all ages. More cycles and longer treatment time produce more effective destruction but also a higher chance of complications. Table 2 depicts the approximate freezing time for treating different viral warts. Patients should be warned of possible adverse effects which include pain, erythema, swelling, haematoma, scarring and pigmentary changes. Contraindications for cryosurgery are few and include cold urticaria, cold intolerance and Raynaud's phenomenon.

Table 2 Suggested freezing time for different viral warts

Lesion	Freezing time in seconds (approx.)
Common wart	10
Filiform wart	5
Genital wart	5-10
Plantar wart	15-30 or longer depending on thickness of lesion

Phototherapy

Phototherapy refers to treatment of disease by controlled exposure to light of specific wavelengths. Ultraviolet radiation (UVR) is widely used for various skin diseases and works by affecting DNA synthesis and suppressing immune function.² Upon exposure, pyrimidine dimers are formed and if a psoralen (q.v.) is added, it would cause photoadduct formation leading to suppressed DNA synthesis.

The parts of the UVR spectrum employed for treating skin diseases include broad band UVB (280-320 nm) (BBUVB), narrow band UVB (311-313 nm) (NBUVB), and UVA (320-400 nm). Their comparison is shown in Table 3. The administration of a psoralen (a furocoumarin) prior to UVR treatment refers to photochemotherapy. Most often, it is given 15-120 minutes prior to UVA radiation and is known as Psoralen UVA (PUVA). In treating psoriasis, oral retinoid and topical calcipotriol can increase the efficacy of PUVA. UVR is delivered via a cabinet (total body irradiation) or a compact device targeted to the diseased area. Since an orally taken psoralen needs a few days for complete metabolism, these patients will remain photosensitive during this period and should be advised to avoid sun exposure, wearing proof sunglasses and the use of sunscreen whenever applicable.

Compared with PUVA, UVB phototherapy does not require a psoralen for a therapeutic effect. It was also found that within the UVB spectrum, wavelength 313 nm is most effective for psoriasis. Therefore, NBUVB (311-313 nm) has become more popular since its introduction in 1980s and its efficacy was found to be similar to PUVA and better than BBUVB. The latter is now falling out of favour.

Recently UVA1 (340-400 nm) without psoralen delivered at medium to high dose is used in some European countries for treating some chronic skin conditions such as atopic dermatitis, localised scleroderma, chronic sclerodermoid graft versus host disease.³ Preliminary data showed promising results. Further studies are required to confirm its efficacy and safety profile.



Table 3 Comparison of BBUVB, NBUVB and PUVA

Treatment mode	Wavelength spectrum (nanometres)	Synergistic treatment	Comments
BBUVB	280 - 320	Coal tar Dithranol	Psoralen is not required. Obsolete. More erythemogenic than NBUVB.
NBUVB	311-313	Calcipotriol Retinoid	Psoralen not required. Efficacy similar to PUVA.
PUVA	320-400	Calcipotriol Retinoid	Avoid in pregnancy. Psoralen is required. Adverse effects of orally administered psoralen: nausea, deranged liver function, prolonged photosensitivity.

Diluted steroid wet-wrap

Diluted steroid wet-wrap refers to the application of diluted steroid under an occlusive wet dressing. It is effective for combating widespread atopic dermatitis not responsive to conventional 'open' application of steroid. The material employed includes tubular dressing, emollient and steroid at appropriate dilution. Tubular dressings such as Tubifast or Tubigrip of sizes that fit the treated areas are used. A steroid is compounded with an emollient to achieve a desirable concentration of the steroid. Individual aliquots are accurately made using an electronic balance.

After a tepid bath, the body is pat dried. The diluted topical corticosteroid is applied to the lesional areas, while liberal emollient is applied onto the dry skin. A wet tubular gauze that fits the size of the area to be treated is applied and then followed by an external dry tubular gauze. Given as an out-patient, the wrap can be kept for 8-12 hours. Afterwards, the dressings are removed and this is followed by open application of emollient and/or a topical steroid if appropriate. The procedure has the following advantages: the occlusive effect of the dressings enhances the effect of the highly diluted topical steroid (a dilution as low as 1: 9 can be effective for children); the inner wet dressing cools the skin and reduces itch sensation; and the two tubular dressings provide physical protection against scratching. Given a demonstration at the office, the mother will quickly learn the technique and would usually do it well in about 15 to 20 minutes. The details of a wet-wrap procedure have been described elsewhere.^{4,5}

Electrotherapy

Electrotherapy is the use of an electric current to stimulate a tissue (bone, ligament, tendons, and skin etc.) for purpose of symptom reduction, healing or restoring a lost function. In dermatology, iontophoresis and transcutaneous electrical neural stimulation (TENS) are common forms of treatment belonging to this kind.

Iontophoresis using glycopyrrolate or tap water is effective for reducing sweat output in idiopathic focal hyperhidrosis when topical antiperspirant fails. Iontophoresis is delivered by an electrotherapy machine such as the Dynatron or Drionic. Treatment can be

given over 30 minutes a time and twice weekly for four to six weeks. A suggested treatment mode is a pulsed D.C. with pulse width of 900 ms and a rest period of 100 ms. Current intensity should be turned at the maximum output (3-11 mA in one study) tolerable by the patient. Abraded or eczematous skin should be treated by alternative method till recovery before it is subjected to iontophoresis. Local experience suggested that about one-third of patients who fail topical antiperspirants give very good response.⁶ However, relapse of symptom needing a maintenance treatment of once a week or two weeks does occur. This can be achieved by home treatment using small iontophoretic device. Treatment combined with topical anticholinergic enhances efficacy.

TENS utilising a pulsed electric current generated transcutaneously by a device to excite nerve fibres, is a well recognised form of electrotherapy. It has long been used for pain relief in musculoskeletal disorders but it can also be used to combat itch in a variety of pruritic conditions.^{7,8} The therapeutic mechanism could be partly explained by the Gate Control Theory which hypothesised that the synaptic transmission of nerve impulses evoked from the skin to the central transmission (T) cells in the dorsal horn could be modified (excitatory or inhibitory) by the substantia gelatinosa which acts as a gate control system. Stimulation of fast A fibres as in the case of TENS activates the neurones in the substantia gelatinosa to produce feedback inhibitory impulses on the afferent fibre terminals, and results in reduced activation of the central transmission (T) cells, thus damping down perception of peripheral nerve impulses. The electrotherapy machine used for delivering iontophoresis can be used for TENS too. Alternatively, a portable TENS device can be available for home treatment. The wetted electrode pads are placed around the area where the most intense itch is felt. Treatment can be carried out at a constant current mode, with wave frequency range of 80-100 Hz and pulse width of 200 µs. The current density is adjusted to a maximum tolerable level to the patient without muscle twitching. Avoid placing the electrodes on the sides of neck for this may put the carotid sinuses at risk of inadvertent compression. Treatment-related adverse effects are rare and include erythema, swelling, irritation, numbness, and other altered sensation. One hour daily given for a week can be given as a trial therapy.

Excision/incisional/punch/shave biopsy

Skin biopsy is an integral part of dermatological management. Conventional surgical excision to remove an elliptical tissue for histopathology is frequently done. A vertical conical core of tissue can also be readily harvested via a biopsy punch (usual calibre used from 3-6 mm in diameter) which makes the surgery even simpler. However, these two require suturing. Shaving of a lesion is gaining popularity for it does not require suturing and its cosmetic outcome is also very good.

Lesions suitable for shaving should be flat and superficially located. Examples are seborrheic wart,



actinic keratosis, wart, skin tag, and superficial pigmented naevi. To facilitate shave excision, normal saline is injected beneath the lesion to make it bulge; a curette is then used to scrape a representative portion of the lesion. Curetting helps the operator to assess the approximate depth and possible nature of the lesion.⁹ For an exophytic benign lesion, it will be easily curetted and separated from the underlying healthy dermis. The shaving is then performed using a blade obtained from a longitudinally half-cut razor blade. The author prefers to use a razor blade for shaving due to its flexible curvature that can be adjusted to suit the dimension of the individual lesion. Haemostasis is achieved by applying aluminium chloride solution onto the wound followed by appropriate dressings. Wound heals well within two weeks.

Whichever surgical method is used, the patient should be given clear instructions on the procedure including the possible adverse effects. The patient should also be checked for risk factors such as diabetes mellitus, hypertension, drug allergy and concomitant drug use that would circumvent a smooth surgery. Specimens excised should be sent for histopathology.

Skin flap surgery

A flap is a segment of tissue with its own blood supply partially dissected from its original site to cover a primary defect. Although dermatologists often deal with small lesions, skin flaps are occasionally needed for excision of a large lesion with intended primary closure under acceptable closure tension. Good blood supply and asepsis are important for a successful skin flap surgery. The design of a skin flap is influenced by the blood supply, skin laxity, tension of closure, and location and direction of the scar. Face and scalp are better sites for skin flaps because the blood supply is good. Small flaps can be performed under local anaesthesia by experienced dermatologist in his surgery. Like other forms of surgery, skin flap is a surgical intervention; and the operator must be well acquainted with local anatomy. Prior full patient assessment for fitness and written consent are mandatory. Complications of flap surgery include flap necrosis, haematoma, infection, distortion of tissues and nerve damage for that clinicians must be vigilant.

Plastic tube insertion for splinting ingrowing toenail

Ingrowing toenail (IGTN) is a common condition often presented to family physicians. Conservative practised treatments such as cotton wool pledget insertion, topical antiseptics and antibiotics produce variable improvement with high recurrence. Flexible tube for splinting the nail is a more effective form of conservative treatment for uncomplicated IGTN and was described by the author elsewhere.¹⁰ Briefly, a longitudinally split plastic tube is used as a splint and is made from a suction catheter which is available in most clinics. It is inserted along the affected lateral nail fold to achieve nail plate skirting. The position of the

splint is then secured by a suture which passes through the nail plate only. Pain relief is rapid and the splint can be left for a maximum of eight weeks until inflammation has subsided and normal nail plate growth is ensured. The concept of splinting an IGTN is actually not new. Nail splinting using a nail guard was first reported successful by Wallace et al in 1979. In this study, 56% of patients at 1 year's assessment had no recurrence.¹¹

Conclusion

Dermatologists are internist equipped with good manual dexterity. It is far from truth that they only focus large part of their work to aesthetic procedures. Given these years' development, local dermatologists are now able to perform simple, safe and effective procedures in their offices. The success is mostly attributed to constant upgrading of the dermatology profession; and in part due to evolution of better instrumentation and modern drugs. The availability of inexpensive portable iontophoretic and TENS devices, and the development of a potent, long-acting but safer, new generation topical corticosteroid allowing diluted steroid wet-wrap dressings to be done as a home treatment are evidence of successful evolution. Aesthetic and conventional procedures are not mutually exclusive; dermatologists should keep abreast of current development and surgical skills.

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Comparison of Various Biological Agents in the Treatment of Psoriasis

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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 30 September 2006.

Introduction

In recent years, there has been considerable breakthrough in understanding the pathogenesis of psoriasis as a T cell mediated autoimmune disease. In genetically predisposed individuals, a triggering antigen, the nature of which is still not clear, is captured by Langerhans' cells in the epidermis. The Langerhans' cell migrates into the regional lymph node and presents the antigen to the T lymphocyte. When the antigen-Langerhans' cell complex interacts with the T cell in the lymph node, the T lymphocyte is activated by two co-stimulatory signals 1 and 2. In predisposed individuals, these activated T cells undergo TH1 differentiation into effector memory T cells and selectively traffics back to the skin and releases inflammatory cytokines such as tumour necrosis factor (TNF) alpha. These cytokines act on the epidermal keratinocytes, dermal blood vessels and other inflammatory cells, producing inflammatory responses that result in clinical lesion of psoriasis.

Biologic agents are synthetic proteins designed to block one or more of these specific steps in the pathogenetic pathway. Four targets are aimed:

- Target 1: Inhibiting T cell activation by blocking the co-stimulatory signal 2 (e.g. by efalizumab, alefacept);
- Target 2: Inducing immune deviation from TH1 differentiation to TH2 differentiation in the activated T cell;
- Target 3: Eliminating activated T cells selectively (e.g. by alefacept);
- Target 4: Inhibiting the action of cytokines, especially tumour necrosis factor (TNF) alpha (e.g. by infliximab, etanercept)

Four of these new biologic agents, namely alefacept, efalizumab, infliximab and etanercept are discussed below. Comparison of their modes of actions, clinical uses, efficacy, side effects and precautions are summarized in Table 1.

Alefacept

In psoriasis, the lymphocyte function-associated antigen (LFA)-3 presents on the Langerhans' cell binds to the

CD2 expressed on activated T cell, producing co-stimulating interaction (signal 2) and leads to T cell activation and a cascade of inflammatory response resulting in psoriasis. Alefacept is a recombinant human LFA-3/IgG1 dimeric fusion protein that binds to CD2 receptor expressed on these activated T cells, thus inhibiting T cell activation (Target 1) and proliferation. In addition, it also causes apoptosis and selective elimination of these pathogenic T cells (Target 3) while preserving the naive T cells. In January 2003, Alefacept was approved by FDA of USA for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. It is administered weekly either by intramuscular injection of 15mg or by intravenous bolus injection of 7.5mg. A course of 12 weeks is usually recommended.

In most clinical trials on efficacy of treatment for psoriasis, the widely adopted parameter is the PASI 75 which measures the percentage of patients achieving at least 75% reduction of their Psoriasis Area and Severity Index (PASI) score from the pretreatment baseline. In alefacept, PASI 75 was achieved in 33% of patients after weekly intramuscular injection for 12-week.¹ Similarly, 28% of patients achieved PASI 75 after a 12 week course of once weekly intravenous alefacept injection while a second course further enhanced clinical efficacy up to 40%.² Significant clinical response occurred at around eight weeks after starting treatment.³ The best clinical efficacy occurred approximately six weeks after the last dose.¹ Comparing with other biologics, remission in the responders was long-lasting and at week 24, 24% of patients still remained clear or almost clear without additional therapy and 71% maintained at least PASI 50 (i.e. 50% reduction of PASI as compared with baseline).¹ For those who needed retreatment, a median interval of 10 months (range: 6 to 18) between the last dose to subsequent retreatment was noted.⁴

The most common side effects were pharyngitis, headache, rhinitis and dizziness.^{1,2,3,4} Mild injection site reaction occurred more often in the intramuscular administration^{1,2} while transient chill during the first day of treatment occurred more often in the intravenous route. One of the important side effects is the reduction of circulating T cell counts. Weekly CD4 T lymphocyte



count monitoring is recommended during treatment. Alefacept should be withheld if the CD4 T lymphocyte count is below 250 cells/mL and discontinued if it remains below 250 cells/mL for four weeks. Ten percent and 2% of patients discontinued intravenous alefacept temporarily and permanently because of low CD4 T lymphocyte count⁴ while 4% and none when alefacept was given intramuscularly.¹ The rate of infection requiring hospitalization was 0.9%. Up to date, alefacept has a satisfactory safety profile.

Efalizumab

Efalizumab is a recombinant humanized monoclonal antibody against the alpha subunit of LFA-1 (i.e. the CD11a) expressed on T lymphocytes. It inhibits the interaction between CD11a and the intercellular adhesion molecule (ICAM)-1 expressed on antigen presenting cells hence stopping the co-stimulatory signal 2 (Target 1) that activates the T cells which lead to a sequence of inflammatory events. Efalizumab was approved by FDA in October 2003 to treat moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. It is usually given by subcutaneous injection of single first conditioning dose at 0.7mg/kg followed by weekly dose at 1mg/kg for a course of 12 weeks.

Twenty-two to 29.2% versus 28 to 41% of patients achieved PASI 75 after 12 week treatment with dose of 1mg/kg versus 2mg/kg respectively.^{5,6} Seventy-seven percent of these good responders maintained their improvement when additional 12 week treatment were given.⁶ The improvement occurred as early as four weeks.⁶ Study showed that additional clinical improvement could be achieved by prolonged treatment beyond 12 weeks.⁵ Treatment up to 24 and 60 weeks, which were well tolerated, increased the percentage of patients achieving PASI 75 to 51% and 64% respectively.⁵ However, when stopping treatment, significant clinical relapse is one of the major disadvantages and 0.7% of patients experienced rebound after discontinuation, suggesting long term maintenance therapy with efalizumab is necessary.⁷

Common minor side effects such as flu-like symptoms occurred in 37% of patients during the first few injections.⁸ It can be minimized by the use of reduced conditioning dose in the first injection. More serious side effect of thrombocytopenia was rarely reported.⁷ Monitoring of platelet count is recommended every month initially and then three-monthly during the treatment period and treatment should be stopped if significant thrombocytopenia occurs.

Infliximab

Infliximab is a chimeric monoclonal antibody which binds to transmembrane and soluble TNF alpha. It binds to TNF specifically and blocks its interaction with cell surface receptors (Target 4). Thus, TNF alpha, which is an important mediator secreted by the activated pathogenic T cells, cannot bind with its natural receptors in various sites and the inflammatory response leading to psoriasis ceases. Infliximab is approved for the treatment of Crohn's disease and rheumatoid arthritis by FDA and is currently under review by the authority for other indications including psoriasis. The drug is usually given 3mg/kg to 5mg/kg

by intravenous infusion over two hours at week 0, 2, 6 then every 8 week if maintenance is necessary.

Infliximab is highly efficacious and 72% versus 88% of patients achieved PASI 75 at week 10 after infusion at 3mg/kg versus 5mg/kg respectively.⁹ Almost half of the responders achieved PASI 75 at 4 weeks.⁹ Other studies showed that 40% and 73% of patients receiving 5mg/kg and 10mg/kg infliximab respectively were able to maintain at PASI 50 at week 26.¹⁰ Hence, infliximab could produce a rapid, effective and sustainable effect in the treatment of psoriasis.

Common side effects are mild including headache, pruritus, fatigue and myalgia. Five percent of patients may develop infusion reactions ranging from mild hypotension and allergic reactions to severe anaphylaxis and seizures which usually occur during or within two hours of infusion.¹¹ Serious opportunistic infections such as disseminated or extrapulmonary tuberculosis were reported.^{11,12} Reactivation of latent tuberculosis may develop within the first three to six months after starting treatment. Pretreatment tuberculin test, chest x ray and anti-tuberculosis prophylaxis are recommended before the commencement of infliximab.^{11,12} Infliximab is also contraindicated in patients with moderate to severe heart failure.

Etanercept

Etanercept is a dimeric fusion protein consisting of two TNF receptor components linked to the Fc portion of human IgG. Similar to infliximab, etanercept binds to TNF specifically and blocks its interaction with cell surface receptors (Target 4). In April, 2004, FDA has approved the use of etanercept for the treatment of moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy. It is also approved for treating psoriatic arthritis, rheumatoid arthritis and ankylosing spondylitis. It is given subcutaneously 50mg twice per week usually for a course of 12 weeks, then 50mg once per week for maintenance if necessary.

PASI 75 was achieved in 49% of patients at week 12 and increased to 59% when twice weekly treatment was extended to 24 weeks.¹³ Clinical improvement was evident as early as 2 weeks. The main side effects were upper respiratory infection (57%), injection site reactions (20%), and headache (13%). Eleven percent and 15% reported induction of antinuclear antibodies and anti-double-stranded DNA but full cases of lupus erythematosus are rare.¹⁴

Conclusion

These new biologic agents are exciting additions of armamentarium for the treatment of psoriasis. As compared with the conventional immunosuppressive therapy (e.g. cyclosporin), they seem to have an improved risk-efficacy ratio. Among them, infliximab seems to be highly efficacious while alefacept apparently offers longer remission to responders. Furthermore, some of them (e.g. efalizumab and etanercept) can conveniently be administered by the patients themselves at home. The downside of these new treatments are the need of laboratory monitoring in some agents (e.g. platelet count in efalizumab and CD4 count in alefacept) as well as the potential serious side



effects such as infusion reaction and opportunistic infections (e.g. tuberculosis in infliximab). The cost of all these new therapeutic agents are very high. Further studies are needed to compare the cost-effectiveness of these new agents with the current systemic anti-psoriatic therapies.

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Table 1 summary of four biological agents for the treatment of psoriasis

Biological agent	Alefacept(Amevive™)	Efalizumab(Raptiva™)	Infliximab(Remicade™)	Etanercept (Enbrel™)
Description	Fusion protein of human LFA-3 and Fc portion of Ig G1	Humanized form of murine antibody against CD11a	Chimeric antibody against TNF alpha with a human IgG1 constant domain and murine variable regions	Fusion protein of the Fc of human IgG1 and the extracellular TNF receptor
Mechanism	Block LFA-3/CD2 interaction and selective eliminate activated T cells	Block LFA-1/ICAM-1 interaction and inhibit T cell activation and inflammatory events	Binds soluble and bound TNF alpha and blocks its activities	Binds soluble and bound TNF alpha and blocks its activities
Target of action	Target 1 & 3	Target 1	Target 4	Target 4
FDA indication	Mod to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy (approved Jan 2003)	Mod to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy (approved Oct 2003)	Crohn's disease and RA	Mod to severe plaque psoriasis in adults (approved Apr 2004); psoriatic, rheumatoid and juvenile rheumatoid arthritis, ankylosing spondylitis
Route of administration	Intramuscular or intravenous bolus	Subcutaneous (by patients at home after training)	Slow intravenous infusion over 2 hours	Subcutaneous (by patients at home after training)
Dosing for one course	15mg imi or 7.5mg ivi weekly for 12 weeks	Begin with single dose of 0.7mg/kg sc, then 1mg/kg sc weekly for 12 weeks	3 to 5 mg/kg iv infusion at week 0,2,6.	50mg sc twice a week for 12 week (50mg sc weekly if maintenance)
Time of onset of improvement	~8weeks	~4 weeks	~4weeks	~2 weeks
Relative efficacy: % of patients achieving PASI 75 after a course of 12 week Px	~28-40%	~22 -41% (Increase to 64% if prolonged treatment)	~72-88%	~49% (Increase to 59% if prolonged treatment)
FDA baseline & monitoring	CD4 count (baseline and weekly)	Platelet count monthly, then every 3 months	Screening for latent TB(tuberculin test, CXR) at baseline	None
Side effect	Flu-like symptoms, injection site reaction, transient chill	Flu-like symptoms	Headache, myalgia, infusion reaction, opportunistic infections	Upper respiratory infection, injection site reaction, headache
Contraindication	Hypersensitivity to alefacept; discontinue if CD4<250cells/uL for 4 weeks	Hypersensitivity to efalizumab or any murine or humanized monoclonal antibody	Hypersensitivity to infliximab or murine products; congestive heart failure	Hypersensitivity to etanercept; active infections or sepsis; congestive heart failure; poorly controlled diabetes
Advantage	Long lasting remission	Self administered by patients possible	Highly efficacious	Also effective against psoriatic arthritis; self administered by patient possible
Disadvantage	Need for CD4 count monitoring, withhold if CD4<250cells/uL, discontinue if persists for 4 weeks	Significant relapse after treatment; long term maintenance necessary	Manpower for iv infusion; risk of anaphylactic infusion reaction; risk of serious opportunistic infection	Serious opportunistic infection reported, prior tuberculin test and CXR advisable in TB endemic area
Estimated drug cost (US\$)	~\$10,000 per course depending on dosing	~\$15,000 per year for maintenance treatment	~12,000 per year depending on dosage	~12,000 per year



MCHK CME Programme Self-assessment Questions

Please read the article entitled "Comparison of Various Biological Agents in the Treatment of Psoriasis" by Dr.KH Lau 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 sheet via fax (2865 0345) or by mail to the Federation Secretariat on or before 30 September 2006. 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 following statements concerning treatment of psoriasis by etanercept are correct except:

- Comparing with other biological agents, the onset of clinical improvement is slow.
- Etanercept has a similar mode of action as infliximab.
- It is approved by FDA for the treatment of moderate to severe chronic plaque psoriasis patients who are candidates for systemic therapy or phototherapy.
- The main side effects are upper respiratory tract infection and injection site reactions.
- Induction of antinuclear antibodies and anti-double stranded DNA were reported after treatment with etanercept.

2. The following are relevant side effects of alefacept except:

- Pharyngitis
- Headache
- Rhinitis
- Lymphocytosis
- Injection site reaction and transient chill during the first day of treatment

3. FDA recommends monitoring of the following parameter(s) during treatment with efalizumab:

- Chest X ray
- White cell count
- Tuberculin test
- Platelet count
- All of the above

4. The following are correct modes of action of the biological agents designed to block the specific steps in the pathogenetic pathway of psoriasis except:

- Alefacept inhibits T cell activation by blocking the co-stimulatory signal 2.
- Etanercept binds soluble and bound tumour necrosis factor (TNF) alpha and blocks its action.
- Alefacept eliminates activated T cells selectively.
- Efalizumab induces immune deviation from TH1 to TH2 differentiation in the activated T cell.
- Infliximab inhibits the action of cytokines, especially tumour necrosis factor (TNF) alpha.

5. The following is/are disadvantage of treatment with infliximab in psoriasis:

- High treatment cost.
- Reactivation of latent tuberculosis.
- Potential serious anaphylaxis during drug administration.
- a and c.
- All of the above

6. The following statements concerning the use of alefacept in the treatment of psoriasis are correct except:

- Comparing with other biologics, the remission induced by alefacept is transient and significant clinical relapse is one of the major disadvantages.
- It was already approved by FDA of USA for the treatment of moderate to severe plaque psoriasis in adult patients.
- Alefacept is a recombinant human LFA-3/IgG1 dimeric fusion protein.
- Alefacept is administered weekly either by intramuscular or by intravenous bolus injection.
- The best clinical efficacy usually occurs few weeks after completing the course of treatment.

7. The following biological agent(s) can be administered at home by trained patients themselves:

- Efalizumab
- Infliximab
- Etanercept
- a and c
- all of the above

8. The following statements concerning the use of efalizumab in the treatment of psoriasis are correct except:

- The usual dosage is 1mg/kg weekly for a course of 12 week.
- Long term treatment of efalizumab up to 60 weeks was proven to be safe and well tolerated.
- Comparing with other biologics, remission in the responders was long-lasting and a significant number of patients still remained clear even after stopping treatment.
- It is usually given by subcutaneous injection.
- Additional clinical improvement could be achieved by prolonged treatment beyond 12 weeks with enhanced clinical efficacy.

9. In treating patients with psoriatic arthropathy complicating extensive stable plaque psoriasis, the following biological agent is an FDA approved treatment option:

- Alefacept
- Efalizumab
- Infliximab
- Etanercept
- None of the above

10. Which of the following statement(s) concerning the use of infliximab in the treatment of psoriasis is/are correct:

- It is administered subcutaneously.
- It is given in 50mg twice a week for a course of 12 week.
- It is approved by FDA for the treatment of Crohn's disease and rheumatoid arthritis.
- No laboratory monitoring is required by FDA
- All of the above.



ANSWER SHEET FOR SEPTEMBER 2006

Please return the completed answer sheet to the Federation Secretariat on or before 30 September 2006 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Comparison of Various Biological Agents in the Treatment of Psoriasis

Dr. KH Lau MBBS(HK), FRCP, FHKCP, FHKAM(Med)

Yaumatei Dermatology Clinic, Social Hygiene Service.

1 2 3 4 5 6 7 8 9 10

Name: _____ HKID No. _____ - _____ X X (x)

Signature: _____ Contact TelNo.: _____

Answers to August 2006 issue

Aesthetic Dentistry and Orthodontics

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



64th Annual Meeting of the American Academy of Dermatology, San Francisco Aesthetic Procedure: Botulinum Toxin

Dr. MC Wong MBBS(HK), MRCP(UK)

Yaumatei Dermatology Clinic, Social Hygiene Service



Dr. MC Wong

Medical use of botulinum toxin (BTX) began in the 1950s with Dr. Vernon Brooks. The first study demonstrating therapeutic value of BTX-A that could weaken extraocular muscles in monkeys was published in 1973. In 1979 the FDA granted limited approval to use BTX-A for strabismus and in 1985 this was expanded to include blepharospasm. Since December 1997, an FDA-approved botulinum toxin A source known as Botox has been used.

In 1987, while treating patients for benign essential blepharospasm, Dr. Jean Carruthers noticed that many of the patients had significant improvement of dynamic rhytides in the glabellar region. In 2003, BTX-A was approved for the treatment of glabellar rhytides. Most facial rhytides form perpendicular to the direction of underlying muscular contractions. As skin loses its elasticity with age and photoaging, it does not rebound as well from the constant forces of stress placed upon it and wrinkles form. A good example of this is the pattern of horizontally oriented lines on the forehead. Forehead rhytides form perpendicular to the vertically contracting frontalis muscle. When the facial muscles responsible for creating the wrinkles are not functionally necessary, BTX may be injected to paralyze or weaken them temporarily and ameliorate the lines.

Clostridium botulinum bacteria produce seven serologically distinct types of botulinum neurotoxin (designated as types A, B, C1, D, E, F and G). All subtypes of BTX act as zinc-dependent endoproteases and prevent the release of acetylcholine at the neuromuscular junction of striated muscle fibres causing a flaccid paralysis. Of the known subtypes of BTX, type A appears to be the most potent in humans.

Clinically, muscle weakness is seen approximately 2-4 days following injection, with full paralysis or maximal weakness complete at seven to ten days. The time to onset and maximal efficacy differs between BTX products and may be dose dependent, with more rapid onset following higher doses.

There are two commercial types of BTX-A available, namely Botox and Dysport. Dr. Lowe compared them for the efficacy and tolerability in the treatment of glabellar lines. It was a double-blind randomized pilot study. Subjects were randomly assigned to receive Botox Cosmetic 20U or Dysport 50U. Glabellar line severity was assessed by a blinded investigator

evaluating photography at maximum contraction. It was shown that Botox offers more prolonged efficacy than Dysport when the two products were compared in a 2.5:1 dose ratio (Dysport:Botox). Both were well tolerated. In addition, mean patient ratings of satisfaction with appearance were significantly higher with Botox than with Dysport. Another study using a 4:1 ratio of Dysport:Botox resulted in comparable efficacy between the two products.

For patients receiving BTX, we must rule out patients with neuromuscular diseases, those who are pregnant or those taking any contraindicated medications. We should contain in the consent the possible complications which include ecchymoses, diplopia, eyelid ptosis, brow ptosis, lateral eyebrow elevation, lower eyelid swelling, muscle weakness and dysphagia. For eyelid ptosis, it occurs because of diffusion of BTX through orbital septum usually from corrugator injection. The incidence is about 0.5-5% with an onset of 2-15 days after injection. The effect usually lasts 2-6 weeks which could be improved with adrenergic agonists eye drops. For brow ptosis, it can be seen with glabellar injection resulting in frontalis muscle weakness. We should be aware that 40-80% of women have brow asymmetry and therefore pre-operative photo-documentation is important. Dysphagia is a rare but serious complication resulting from diffusion of BTX from platysmus injection.

BTX injections are now reported to be the most common cosmetic procedure performed in the United States. Although results are not long term, BTX injections provide outstanding clinical results for a variety of facial rhytides with almost no down time. As people continue to seek less invasive treatments for the signs of aging, the use of BTX is likely to continue to rise.



64th Annual Meeting of the American Academy of Dermatology, San Francisco Advances in Photomedicine: Photodynamic therapy

Dr. JTHT Yu BM BCh(Oxon), MRCP(UK)

Yaumatei Dermatology Clinic, Social Hygiene Service



Dr. JTHT Yu

Background

Sunlight had been used to treat skin diseases for centuries. As early as 1400 BC, there had been documentations on the use of photodynamic therapy (PDT) in Egypt when people with vitiligo were given certain plant extracts and then exposed to the sun for treatment. In 1911, Hausman described the ability of light-activated hematoporphyrin to photosensitize guinea pigs and mice. In 1913 Meyer-Betz showed that hematoporphyrin could photosensitize humans by injecting himself with hematoporphyrin and noting swelling and pain in parts of his body exposed to sunlight. However, Meyer-Betz also endured skin phototoxicity for 2 months, which was a major drawback in the use of hematoporphyrin as a photosensitizer¹.

To overcome the prolonged risk of phototoxicity, Kennedy and colleagues² introduced topically applied 5-aminolevulinic acid (ALA) in 1990. ALA is a photosensitizing "prodrug" that can penetrate the stratum corneum of abnormal cells and is converted to protoporphyrin IX (PpIX) in the skin. PpIX is subsequently activated by an appropriate light source. Since then, photodynamic therapy (PDT) has been applied to almost every type of cutaneous cancer and numerous skin disorders e.g. actinic keratosis, superficial basal cell carcinoma, Bowen's disease, patch and plaque stage mycosis fungoides, psoriasis, acne vulgaris and photorejuvenation. In the United States, the Food and Drug Administration (FDA) only approved the use of PDT in the treatment of non-hypertrophic actinic keratosis of the face and scalp with delta aminolevulinic acid (Levulan Kerastick™, Dusa Pharmaceuticals, Inc.) after a 14 hour to 18 hour skin contact time and activation with a blue light source (417 nm).

Mechanisms

PDT requires the presence and interaction of three components: photosensitizer, light, and oxygen. ALA must penetrate the stratum corneum of the target area and ALA-induced PpIX must accumulate in sufficient quantity to have a therapeutic effect. Fluorescence studies show that ALA penetration decreases with skin thickness and increases in the presence of photo-damage and other skin abnormalities such as actinic

keratosis, psoriasis and basal cell carcinoma. Once inside, ALA diffuses through the epidermis into the dermis but despite that, very little PpIX is actually found in the dermis as demonstrated in fluorescence studies. As a result, ALA PDT can eradicate epidermal cancers without seriously damaging the dermis, thus avoiding scarring². The time for ALA to diffuse to 3.0 mm from the skin surface has been estimated to be between 3 hours to 15 hours.

When enough PpIX has accumulated, the treatment area is exposed to the wavelengths of light absorbed by PpIX. In general, the longer the wavelength, the deeper its penetration. In PDT, activation of photosensitizer generates products that can destroy cells. The primary cytotoxic agent is believed to be singlet oxygen, a metastable intermediate produced, when photosensitizer is activated. Cell death has been shown to involve an apoptotic mechanism. In the treatment of skin cancer with PDT, vascular injury also plays an important role in tumour destruction as PDT induces changes in both tumour and surrounding microvasculature.

Treatment of Actinic Keratosis

Actinic keratosis is considered by some to be an in situ cancer. Although the natural history of a specific lesion is unpredictable, all actinic keratosis should be treated to avoid progression to squamous cell carcinoma. Different experiments with a variety of light sources including blue light (417 nm), red light (635 nm), pulsed dye laser and intense pulsed light (IPL) had been shown to activate PpIX with ALA incubation times ranging from 3 hours to 24 hours.

In most cases, cure rates for actinic keratosis lesions exceeded 75% with a single treatment. Adverse effects included localized oedema and erythema as well as mild stinging and burning sensation during treatment. The recurrence rate of actinic keratosis lesions treated with ALA PDT had been studied by Fowler and colleagues³ and they reported that four years after treatment, 69% out of 32 lesions in four patients were still clear, 9% recurred, and 22% were "uncertain." Having established the safety and efficacy of ALA PDT, more research has been done to make the procedure more practical^{4,5}. These studies collectively showed that short-contact (30 minutes) and wide field ALA PDT



provides efficacy and safety in the treatment of non-hypertrophic actinic keratosis. In addition to the treatment of actinic keratosis, improvement on the skin texture of the patients treated with ALA PDT had also been noted by the investigators and they proposed that ALA PDT may be used as a form of non-ablative skin rejuvenation. In another study, PDT with one hour ALA incubation and blue light activation had been shown to clear actinic keratosis as effectively as topical 5-fluorouracil⁶.

In general, the number of treatments depends upon clinical indication and response. Usually, two to five treatments will be given at four week apart. It is important to vary drug incubation time and fluence to achieve desired clinical response. Resolution of actinic keratosis correlates directly with the amount of post-treatment redness and peeling. Although responses vary among patients, the absence of redness for 48 hours after treatment generally indicates that the ALA incubation time was insufficient to achieve the therapeutic level, and that the ALA incubation time should be increased. Alternatively, higher penetration of ALA could also be achieved with a more vigorous skin preparation that removes the keratin layer before incubation, e.g. microdermabrasion and acetone scrub. With more aggressive treatment regime, fewer treatment sessions are required to achieve the same clinical endpoint. Therefore, ALA incubation time may be gradually increased from 30 minutes to 90 minutes, depending on the patient's tolerance.

PDT is useful in the treatment of actinic keratosis because it can offer field treatment in addition to the treatment of individual lesions. However, it may not work as well on thicker lesions. Common side effects include pain, erythema, crusting, blistering and post-inflammatory hyperpigmentation. The treatment parameters, such as the type and dosage of photosensitizer, light device, fluence, and number of PDT sessions can vary according to the clinical response. In Asian skin, post-inflammatory hyperpigmentation is relatively common and therefore, less aggressive regime is more suitable.

Suggested Treatment Algorithms

Pre-Treatment Care

1. Continue other topical or systemic medications as required.
2. For patients with thick actinic keratosis, consider treating with a short course of imiquimod or 5-fluorouracil beforehand.

Treatment Protocol

1. Wash area to be treated with soap, water and alcohol.
2. Perform single pass microdermabrasion, and scrub area with acetone.
3. Prepare 20% ALA by crushing ampoules and shaking the Kerastick for three minutes.
4. Apply ALA liberally but avoid the mucous membranes.
5. Allow ALA to incubate for at least 30 minutes.

6. Remove ALA with soap and water and wipe with alcohol.

7. Apply appropriate light sources. For example, apply blue light (417 nm) for 15 minutes as a single light source or 5 minutes when used in combination with IPL.

Post-treatment Care

1. During the whole course of treatment, apply titanium dioxide or zinc oxide sun-block with a sun-protection factor (SPF) of at least 30.
2. Instruct patient to avoid direct sun exposure for 48 hours immediately after PDT.
3. Tell patient to expect desquamation and sunburn-like reaction with mild to moderate redness and erythema for up to 72 hours.
4. Apply moisturizers liberally.

Conclusions

PDT is a safe and effective modality for the treatment of non-hypertrophic actinic keratosis. Since downtime is minimal, the technique is suitable for patients of all ages and lifestyles. Additional cosmetic benefit is also seen but as post-inflammatory hyperpigmentation is a major problem in Asian skin, sun protection is extremely important.

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Clinical Quiz

Dr. Helen KS Tung

Associate Consultant, Department of Radiology, Queen Mary Hospital



Dr. Helen KS Tung



Clinical History

This is a KUB film of a 60-year-old man who presented with hypertension and occasional flank pain.

Question:

- What do you see on the KUB film?
- What is the likely diagnosis and how would you confirm your diagnosis?

(See P. 25 for answers)

CALL FOR SUBMISSION OF ARTICLES FOR PUBLICATION IN THE HONG KONG MEDICAL DIARY



The Editorial Board of the Hong Kong Medical Diary invites you to send in your interesting articles for publication in the Hong Kong Medical Diary (500 -1,500 words per article). Abstracts from recent local or international meetings/symposia are also welcome. You can send in your manuscript by facsimile at 2865 0345, through mail or via email at sue.cheng@fmshk.org. The Editorial Board of the Hong Kong Medical Diary will give you a prompt reply.



Medicine and Music

Dr. HC Fung MBChB(Manc), FHKCP, FHKAM(Med)

Private Dermatologist



Dr. HC Fung

As a humble dermatologist and music lover, I am most honoured to be asked by my senior colleague and friend Dr. L.Y. Chong to write something interesting about Music and Medicine, the two big Ms in my life: one my career, the other my favourite hobby. Actually to be a musician (professionally) is much harder to achieve than a medical doctor. To be a doctor, you don't need to be a genius although it helps, but music demands a talented mind, especially helpful if you happen to be a genius or at least somebody approaching that calibre. Music helps us to relax and immerse ourselves in its artistry, experiencing the emotion and to be touched by its inner feelings. It is God's gift to mankind. I know a number of eminent surgeons preferring to use some music as a background when they embark on difficult operations or using music to relax their patients during operation. Talking about musical instruments, the best is usually costly, e.g. the Italians make the best violins in general and the French interestingly make the best violin bows. For pianos, the best is Bozendorfer (Austria); Steinways (USA or German made); or Fazioli (Italian). Bozendorfer has innate naturalness and sweetness about it, but the big models can also sound wonderfully powerful, classy and charming. It seems able to communicate inner feeling better than the Steinways whereas the big Steinways are more powerful with more extrovert personality, therefore more suitable as a concert piano used in big concert halls. Steinways also have a brighter tone than Bozendorfer. Therefore some famous pianists like to use Bozendorfer as self use but use Steinways as concert instruments. The famous pianist Horowitz even travels with his favourite Steinway. Fazioli is also a famous Italian concert piano. In general, it sounds more powerful and resonant even more than the Steinways but needs a heavy hand to produce sound. Tone colour is neutral, quite sweet and has its own personality. Music is just like medicine, the more you experience it, the better you will get acquainted with it. Just like the more patients you see, the more experienced doctor you will make of you. Therefore, never give up a chance to hear more concerts or hear more CDs or more radio broadcasts. Radio 4 of RTHK FM 97.6 to 98.9 is a good place to start listening to classical music and moreover, it is free as long as you have a radio that can receive FM broadcast. If you like a particular composer, in addition to listening to more of his/her compositions, you can also learn a lot about his/her by studying their biographies or personal letters. Recently, I embark on reading Mozart's letters

to his father, mother and sister. It makes fascinating reading and let me know more about the man himself, how he thinks, what is his personal philosophy, the background of his contemporary fellows and so on. By doing this, I believe you can appreciate that composer's music much more. As for Mozart, it is actually quite difficult NOT to like his music and I recommend this composer to anybody who is a beginner in classical music to listen to his music, for it will give a good general introduction to the classical music world. Mozart wrote all sorts of music including chamber, solo instrument, organs, concertos, symphonies, operas, etc. There is not a single repertoire that he didn't venture into and excel in it.

What about musicians and medicine or medical people? History is full of interesting stories about these. For example, do you know that Tchaikovsky is a homosexual? In his time, which was orthodox Tsarist Russia, this was not permitted. Rumour had it that he had liaised with some of the Tsar's relatives in sexual matters therefore he was eventually drawn to suicide. It was interesting to note that he did his best once to try to hide his homosexuality by marrying one of his students only to end his marriage in disaster and suffering mental breakdown as a result. On the other hand, everybody knew that Beethoven was not too friendly at times! Contemporary people found him quite abrupt and down right rude at times. It is only by advancement of modern medical science recently that by analyzing his skull bone, one finds that he actually suffered from chronic lead poisoning due to large amount of lead used in beverage containers, and water pipes in Beethoven's time. No wonder the poor soul always complained to his physicians that he had constant bad headache, abdominal bloating and colic, in addition to neural damage causing permanent deafness. Yet despite all these difficulties and great personal agony, the man could still produce astonishing works of great beauty and majesty. The discovery of lead poisoning in Beethoven was recently made into a film documentary and aired in ATV when I watched it a couple of weeks ago. What about the association of medical men with musicians? Of course, there are good examples: one of these is the dedication of some of Brahms's quartets to the great Austrian surgeon Billroth (of Billroth gastric surgery fame). Apparently, they were very good friends. The Rachmaninov 2nd piano concerto is one of the most romantic piano concertos ever written. The story had it that Rachmaninov



suffered mental depression after harsh criticism of his 1st symphony. It was through a kind and supportive psychiatrist friend's therapy that he was able to recover completely from his mental illness and started to compose again. Hence he dedicated the 2nd piano concerto to this doctor friend as a sign of gratitude. In fact, the psychotherapy used by the good doctor was a simple yet effective phrase that he asked Rachmaninov to repeat 3 times each day to himself "I am the greatest composer of my time!!"

It would be nice to hear as many concerts as possible in one's life time to enhance one's cultural life. But in practicality, sometimes it is not possible due to busy clinical practice and sometimes we feel just too tired to go to concerts after a hard day's work. Hence a good HiFi system is essential so one could hope to emulate or bring the concert hall experience to one's home so to speak. The better your HiFi system, the better you should feel the experience about this real living concert performance. First, we must acquaint ourselves with the true sound of the instruments, Jazz bands or human voice. Therefore one should start by going to concerts to hear what a real instrument, or what Jazz band, or human voice sound like. Once you have the mental picture of the real thing, you should be able to make less mistakes by creating a genuine HiFi system that will approximate the real life experience.

Some rough guidelines are as follows:

1. One should spend more money on the source be it a CD player, tuner (for radio broadcast) or LPD (long

playing disc) system because if you start with an inferior source, it would not be accurate because the signal will be amplified even worse than it already is down the HiFi chain, e.g. amplifier, cable and loudspeakers.

2. Hear as many prospective HiFi systems (within your budget) as possible before committing to buying. Therefore, go to HiFi Shows and hear friend's HiFi systems. For examples, if you like Jazz, the 1st thing is to go to listen to the Jazz band live, buy a CD of the same performance and test the CD on the various prospective HiFi systems so you will be able to shortlist a few systems that closely match the real life sound experience. In that case you will not be too far wrong.
3. Talk to experienced friends, musicians, sound engineers (some of my best friends are recording engineers) to get an objective input so you can shop wisely.
4. In general, if you play your favourite CDs for a long period on your chosen system and do not feel tired, it is a good system because it encourages you to keep playing your favourite discs! I also sometimes tell my HiFi friends that if you feel emotionally connected to the music through your HiFi system, whether it is sad or happy, it is a good system for you and you only; never mind what other people say or think about your system because it is THE system you have "to live with" day and night! Just like living with your wife or girl friend.

Answer to Clinical Quiz

Radiographic Findings

Bilateral renal shadows are enlarged. Multiple ring-shaped and curvilinear calcifications are present diffusely in both renal shadows.

Diagnosis:

Autosomal dominant polycystic renal disease.

Definitive diagnosis is established by ultrasound, which will show typical finding of multiple cysts of varying size in the enlarged kidneys. Ultrasound would also be able to detect complications of these cysts such as haemorrhage, infections, cyst wall calcifications and renal calculus disease.

Dr. Helen KS Tung

Associate Consultant, Department of Radiology, Queen Mary Hospital



Soccer Five Tournament 2006

Match results for 30 July 2006

HKOS	2 : 1	Sanofi-Aventis
Jacobson	5 : 3	Eli Lilly
HKDA	9 : 0	Wyeth
Abbott	0 : 4	T. Mountain

Match on 24 June 2006

There were 4 exciting matches between medical societies and pharmaceutical companies on 30th July 2006. The most outstanding performance was by The Hong Kong Dental Association who got the highest score on that day; on the other hand, it was a "Black Sunday" for the pharmaceutical companies since they all lost. We hope they can achieve better results next time.



The Hong Kong Dental Association team from left to right: Dr Anthony Lam, Dr Leung Yiu Yan, Dr Liu Wing Hong, Dr Frank Mok and Dr Marco Lau



Society News

News from Member Societies

Hong Kong Association for the Study of Liver Diseases

New office-bearers for the year are as follows: President: Dr. Henry Lik-yuen CHAN, Hon. Secretary: Dr. Steven Woon-choy TSANG.

Hong Kong Urological Association

New office-bearers for the year are as follows: President: Dr. Wai-sang WONG, Hon. Secretary: Dr. Shu-keung LI, Council Representative: Dr. Wai-sang WONG.

The Guild of St. Luke

New office-bearers for the year are as follows: Master: Dr. Peter AU YEUNG, Hon. Secretary: Dr. Michael POON, Assistant Hon. Secretary: Dr. Stella Pui-yan WONG, Honorary Treasurer: Dr. Francis CHU

The Hong Kong Medical Association

New office-bearers for the year are as follows: President: Dr. Kin CHOI, Vice-Presidents: Dr. Kin-wah CHU, Dr. Tai-cho SHIH, Hon. Secretary: Dr. Chi-chiu LEUNG, Hon. Treasurer: Dr. Pak-chin CHOW, Immediate Past President: Dr. Wing-lok LO.

The Hong Kong Neurological Society

New office-bearers for the year are as follows: President: Dr. Raymond Tak-fai CHEUNG, Vice-President: Dr. Tak-hong TSOI, Hon. Secretary: Dr. Jonas Hon-ming YEUNG, Hon. Treasurer: Dr. Leonard Sheung-wai LI.

The Hong Kong Society of Haematology

New office-bearers for the year are as follows: Chairman: Dr. Clarence Chun-kit LAM, Hon. Secretary: Dr. Michael Lap-gate WONG, Hon. Treasurer: Dr. Albert Kwok-wai LIE.

The Hong Kong Society of Occupational and Environmental Medicine

New office-bearers for the year are as follows: Chairperson: Dr. Mang-ye HO, Vice-chairman: Dr. Chor-yiu CHOW, Hon. Secretary: Dr. Hon-keung CHAN, Hon. Treasurer: Dr. Yuen-kong WAN, Council Representative: Dr. Hon-keung CHAN.

The Society of Anaesthetists of Hong Kong

New office-bearers for the year are as follows: President: Dr. Steven Ho-shan WONG, Hon. Secretary: Dr. Ha-yun LEE, Council Representative: Dr. Chi-wai CHEUNG.

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

Welcome New Members

The FMSHK would like to welcome Hong Kong Society for Paediatric Immunology and Infectious Diseases as ordinary member of the FMSHK.



Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
<ul style="list-style-type: none"> ★The Federation's Soccer Five Tournament 2006 <p style="text-align: center;">3</p>	<ul style="list-style-type: none"> ★Certificate Course on Updates in Cervical Cancer Prevention C109 <p style="text-align: center;">4</p>	<ul style="list-style-type: none"> ★家務助理陪月服務訓練課程 (TC-PNC-0106) ★Certificate Course on Childhood Epilepsy C102 <p style="text-align: center;">5</p>	<ul style="list-style-type: none"> ★HKMA Golf Tournament ★保健員深造課程 (藥物學) (TC-AHW-0106) <p style="text-align: center;">6</p>	<ul style="list-style-type: none"> ★HKMA Council Meeting ★家務助理陪月服務訓練課程 (TC-PNC-0106) <p style="text-align: center;">7</p>	<ul style="list-style-type: none"> ★Certificate Course on Orthoptics C105 (PTH06/01) ★Workshop on Intractable Epilepsy in Paediatrics <p style="text-align: center;">1</p>	<ul style="list-style-type: none"> ★8th Joint Annual Scientific Meeting ★Workshop on Intractable Epilepsy in Paediatrics <p style="text-align: center;">2</p>
<ul style="list-style-type: none"> ★HKMA Structured CME Programme at Queen Elizabeth Hospital Year 06/07 (VI) - Orthopaedics ★HKMA Badminton Tournament ★2006 Paediatric Update No.2 - Early Infant Feeding <p style="text-align: center;">10</p>	<ul style="list-style-type: none"> ★Certificate Course on Updates in Cervical Cancer Prevention C109 <p style="text-align: center;">11</p>	<ul style="list-style-type: none"> ★The Origin and History of OGSHK and Stories of The Nineteen Sixties ★Task Force on the Exercise for Health Meeting ★HKMA Newsletter Editorial Meeting ★家務助理陪月服務訓練課程 (TC-PNC-0106) ★Certificate Course on Childhood Epilepsy C102 <p style="text-align: center;">12</p>	<ul style="list-style-type: none"> ★Hong Kong Neurosurgical Society Monthly Academic Meeting - Intra-cranial Sinus Thrombosis ★保健員深造課程 (藥物學) (TC-AHW-0106) <p style="text-align: center;">13</p>	<ul style="list-style-type: none"> ★HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2006 (IX) - One Stop Diagnosis of Infertility ★The Dark Side of Prosthodontic Treatment ★家務助理陪月服務訓練課程 (TC-PNC-0106) <p style="text-align: center;">14</p>	<ul style="list-style-type: none"> ★Certificate Course on Orthoptics C105 (PTH06/01) <p style="text-align: center;">15</p>	<ul style="list-style-type: none"> ★Pre-hospital Trauma Life Support (PHTLS) Provider Course ★Trailwalker Practice Session <p style="text-align: center;">16</p>
<ul style="list-style-type: none"> ★Pre-hospital Trauma Life Support (PHTLS) Provider Course <p style="text-align: center;">17</p>	<ul style="list-style-type: none"> ★Certificate Course on Updates in Cervical Cancer Prevention C109 <p style="text-align: center;">18</p>	<ul style="list-style-type: none"> ★家務助理陪月服務訓練課程 (TC-PNC-0106) ★Certificate Course on Childhood Epilepsy C102 <p style="text-align: center;">19</p>	<ul style="list-style-type: none"> ★Certificate Course for Clinic Nurses C100 ★保健員深造課程 (藥物學) (TC-AHW-0106) <p style="text-align: center;">20</p>	<ul style="list-style-type: none"> ★家務助理陪月服務訓練課程 (TC-PNC-0106) <p style="text-align: center;">21</p>	<ul style="list-style-type: none"> ★Certificate Course on Orthoptics C105 (PTH06/01) <p style="text-align: center;">22</p>	<ul style="list-style-type: none"> ★The Federation's Soccer Five Tournament 2006 <p style="text-align: center;">23</p>
<ul style="list-style-type: none"> ★Trailwalker Practice Session ★12th Annual Scientific Meeting ★HKMA Badminton Tournament ★HKMA Structured CME Programme at Kwong Wah Hospital Year 06/07 (VI) - Medicine ★HKMA Tennis Tournament ★The Federation's Soccer Five Tournament 2006 <p style="text-align: center;">24</p>	<ul style="list-style-type: none"> ★Certificate Course for Development of Advanced Nursing Practice (TC-ANP-0106) ★Management Interest Group Seminar on "Stress Management" ★Certificate Course on Updates in Cervical Cancer Prevention C109 <p style="text-align: center;">25</p>	<ul style="list-style-type: none"> ★家務助理陪月服務訓練課程 (TC-PNC-0106) ★Certificate Course on Childhood Epilepsy C102 <p style="text-align: center;">26</p>	<ul style="list-style-type: none"> ★保健員深造課程 (藥物學) (TC-AHW-0106) ★Certificate Course for Clinic Nurses C100 <p style="text-align: center;">27</p>	<ul style="list-style-type: none"> ★醫藥護理英語基礎課程 (TC-FEC-0106) ★家務助理陪月服務訓練課程 (TC-PNC-0106) <p style="text-align: center;">28</p>	<ul style="list-style-type: none"> ★Certificate Course on Quality Management (TC-CQM-0106) ★初級醫學普通話課程 (PTH06/01) <p style="text-align: center;">29</p>	<ul style="list-style-type: none"> ★HKMA Tennis Tournament ★The Federation's Soccer Five Tournament 2006 <p style="text-align: center;">30</p>



Date / Time	Function	Enquiry / Remarks
1 FRI 7:00pm - 8:30pm (8,15,22)	Certificate Course on Orthoptics C105 Organised by: The Federation of Medical Societies of Hong Kong & Hong Kong Orthoptists Association Speaker: Various # Lecture Hall, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Karen CHU Tel: 2821 3515 Fax: 2865 0345
	初級醫學普通話課程 (PTH06/01) Organised by: The Federation of Medical Societies of Hong Kong # Lecture Hall, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Karen CHU Tel: 2821 3515 Fax: 2865 0345
	10:00am - 8:30pm (2) Workshop on Intractable Epilepsy in Paediatrics Organised by: Dept. of Diagnosis Radiology/TMH, Dept. of Paed/TMH, Dept. of Neuro/TMH & Hong Kong Epilepsy Society & The Hong Kong Neurosurgical Society Speaker: Dr. Simon HARVEY & Dr. K.L. YAM # TMH & HAHO	Ms. Shirley MA Tel: 2468 5402 Fax: 2456 9000
2 SAT 1:00pm - 6:30pm	8th Joint Annual Scientific Meeting Organised by: The Hong Kong Society of Gastroenterology, Hong Kong Society of Digestive Endoscopy, Hong Kong Society for Coloproctology, The Hong Kong Association for The Study of Liver Diseases & The Hong Kong Society of Gastrointestinal Motility Chairman: Dr. M.F. YUEN Speaker: Various # Meeting Room 201, Hong Kong Convention & Exhibition Centre, Wanchai, Hong Kong	Mr. Audrey LAU & Ms Vicky LEE Tel: 2869 5933 Fax: 2869 9533
3 SUN (23,24)	The Federation's Soccer Five Tournament 2006 Organised by: The Federation of Medical Societies of Hong Kong & The Hong Kong Association of the Pharmaceutical Industry Chairman: Dr. Godfrey C.F. CHAN # Shek Kip Mei Park Sports Centre, 290 Nam Cheong Street, Shek Kip Mei, Sham Shui Po	Ms. Karen Chu Tel: 2821 3515 Fax: 2865 0345
5 TUE 6:00pm - 9:00pm (7,12,14,19,21,26,28) 7:15pm - 8:45pm (12,19,26)	家務助理陪月服務訓練課程 (PTH06/01) Organised by: College of Nursing, Hong Kong Speaker: Various	Sugar Tel: 2572 9255 Fax: 2838 6280
	Certificate Course on Childhood Epilepsy C102 Organised by: The Federation of Medical Societies of Hong Kong & The Hong Kong Society of Child Neurology & Developmental Paediatrics Speaker: Various # 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Karen CHU Tel: 2821 3515 Fax: 2865 0345
6 WED 11:00am 6:00pm - 9:00pm (13,20,27)	HKMA Golf Tournament Organised by: Hong Kong Medical Association Chairman: Dr. W LI & Dr. L HOU # Jockey Club Kau Sai Chau Public Golf Course, Kau Sai Chau, Sai Kung, New Territories	Ms. Dora HO Tel: 2527 8285
	保健員深造課程 (藥物學) (TC-AHW-0106) Organised by: College of Nursing, Hong Kong Speaker: Various	Sugar Tel: 2572 9255 Fax: 2838 6280
7 THU 8:00pm	HKMA Council Meeting Organised by: The Hong Kong Medical Association # HKMA, Headquarter Office, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong	Ms. Christine WONG Tel: 2527 8285
9 SAT 9:00pm - 6:30pm (17) 7:30pm	Pre-hospital Trauma Life Support (PHTLS) Provider Course Organised by: Department of Surgery, University of Hong Kong and Hong Kong Chapter of the American College of Surgeons # Room 703, St. John Tower (2 Macdonnell Road, Hong Kong)	Course Secretariat Tel: 2530 8016
	Trailwalker Practice Session Organised by: The Hong Kong Medical Association Chairman: Dr. C YU # St. Teresa's Hospital, Main Foyer	Ms. Dora HO Tel: 2527 8285
10 SUN 2:00pm 2:00pm 2:00pm - 5:00pm	HKMA Structured CME Programme at Queen Elizabeth Hospital Year 06/07 (VI) - Orthopaedics Organised by: The Hong Kong Medical Association & Queen Elizabeth Hospital Chairman: Dr. T.C. SHIH Speaker: Various # Multi-Function Room, Block D, G/F, Queen Elizabeth Hospital	Miss Nina HUNG Tel: 2861 1979 (Registration fee is required) 3 CME Points
	HKMA Badminton Tournament Organised by: The Hong Kong Medical Association Chairman: Dr. C.F. YEUNG & Dr. S.N. CHEONG # MacLehose Medical Rehabilitation Centre, Shop 148, 1/F, Olympian City, 18 Hoi Ting Road, West Kowloon	Ms. Dora HO Tel: 2527 8285
	2006 Paediatric Update No.2 - Early Infant Feeding Organised by: Hong Kong College of Paediatricians Chairman: Dr. Shirley LEUNG Speaker: Various # HAHO, M Floor, Lecture Theatre	Ms. Jenny CHAN Tel: 2871 8871 Fax: 2785 1850 3 CME Points
11 MON 7:00pm - 8:30pm (18,25)	Certificate Course on Updates in Cervical Cancer Prevention C109 Organised by: The Federation of Medical Societies of Hong Kong & The Hong Kong Society of Colposcopy & Cervical Pathology Speaker: Various # Lecture Hall, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Karen CHU Tel: 2821 3515 Fax: 2865 0345
12 TUE 7:00pm - 10:00pm 8:00pm 8:00pm	The Origin and History of OGS HK and Stories of The Nineteen Sixties Organised by: The Obstetrical and Gynaecological Society of Hong Kong Chairman: Dr. LAM Siu Keung Speaker: Prof. LEE Kin Hung # The Ballroom, 3/F, Sheraton Hong Kong Hotel and Towers, Tsimshatsui, Kowloon	Miss Teresa CHAN Tel: 2510 6310 Fax: 2969 5511 1 CME Point
	Task Force on the Exercise for Health Meeting Organised by: The Hong Kong Medical Association Chairman: Dr. Y.S. CHAN & Dr. C.F. YEUNG # HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Miss Maggie HUI Tel: 2527 8285
	HKMA Newsletter Editorial Meeting Organised by: The Hong Kong Medical Association Chairman: Dr. H.H. TSE # HKMA Headquarter Office, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong	Ms. Tammy TAM Tel: 2527 8941
13 WED 7:30AM	Hong Kong Neurosurgical Society Monthly Academic Meeting - Intra-cranial Sinus Thrombosis Organised by: Dr. Y.C. PO, Hong Kong Neurosurgical Society Chairman: Dr. PANG Kai Yuen Speaker: Dr. WONG Kai Sing Alain # Seminar Room, G/F, Block A, Queen Elizabeth Hospital	Dr. Y.C. PO Tel: 2990 3788 Fax: 2990 3789 2 CME Points
14 THU 2:00pm	HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2006 (IX) - One Stop Diagnosis of Infertility Organised by: The Hong Kong Medical Association and Hong Kong Sanatorium & Hospital Chairman: Dr. T.C. SHIH Speaker: Dr. K.H. LEONG # HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Miss Nina HUNG Tel: 2861 1979 (Registration fee is required) 1 CME Point



Date / Time	Function	Enquiry / Remarks
14 THU 7:10pm - 8:40pm	The Dark Side of Prosthodontic Treatment Organised by: Hong Kong Dental Association Chairman: Dr. George LEUNG Speaker: Dr. Patrick WU # Sung Room, 4/F Sheraton Hong Kong Hotel, Tsimshatsui, Kowloon	Ms. Anna WU Tel: 2528 5327 Fax: 2529 0755 1.5 CME Points
20 WED 1:30pm - 3:00pm (27)	Certificate Course for Clinic Nurses C100 Organised by: The Federation of Medical Societies of Hong Kong Speaker: Various # Lecture Hall, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Karen CHU Tel: 2821 3515 Fax: 2865 0345
24 SUN 8:00am 9:00am - 4:45pm 2:00pm 2:00pm 7:30pm	Trailwalker Practice Session Organised by: The Hong Kong Medical Association Chairman: Dr. C YU # Pak Tam Chung (Tuck Shop) 12th Annual Scientific Meeting Organised by: The Hong Kong Society of Rheumatology Chairman: Dr. H.S. TSUI & Dr. K.W. LEE Speaker: Various # Ballroom, Langham Hotel, 8 Peking Road, Tsimshatsui HKMA Badminton Tournament Organised by: The Hong Kong Medical Association Chairman: Dr. S.N. CHEONG # MacLehose Medical Rehabilitation Centre, Shop 148, 1/F, Olympian City, 18 Hoi Ting Road, West Kowloon HKMA Structured CME Programme at Kwong Wah Hospital Year 06/07 (VI) - Medicine Organised by: The Hong Kong Medical Association and Kwong Wah Hospital Chairman: Dr. T.C. SHIH Speaker: Various # Lecture Theatre, 10/F, Yu Chun Keung Medical Memorial Centre, Kwong Wah, Hospital HKMA Tennis Tournament Organised by: The Hong Kong Medical Association Chairman: Dr. C.W. CHIN # Kowloon Tong Club, 113A Waterloo Road, Kowloon Tong, Kowloon, Hong Kong	Ms. Dora HO Tel: 2527 8285 Ms. Teresa LEUNG Tel: 2599 8280 Fax: 2599 8998 Ms. Dora HO Tel: 2527 8285 Miss Nina HUNG Tel: 2861 1979 (Registration fee is required) 1 CME Point Ms. Dora HO Tel: 2527 8285
25 MON 6:00pm - 9:00pm 6:30pm - 8:00pm	Certificate Course for Development of Advanced Nursing Practice (TC-ANP-0106) Organised by: College of Nursing, Hong Kong Speaker: Various Management Interest Group - Seminar on "Stress Management" Organised by: College of Nursing, Hong Kong Speaker: Dr. Alex CHEUNG	Sugar Tel: 2572 9255 Fax: 2838 6280 35 CME Points Sugar Tel: 2572 9255 Fax: 2838 6280 1.5 CME Points
28 THU 6:00pm - 9:00pm	醫療護理英語基礎課程 (TC-FEC-0106) Organised by: College of Nursing, Hong Kong Speaker: Various	Sugar Tel: 2572 9255 Fax: 2838 6280
29 FRI 6:00pm - 9:00pm	Certificate Course on Quality Management (TC-CQM-0106) Organised by: College of Nursing, Hong Kong Speaker: Various	Sugar Tel: 2572 9255 Fax: 2838 6280 35 CME Points



Calendar of Events

Meetings

20-21/10/2006	Scientific Symposium on Emergency Medicine: Meeting a Decade of Challenges Organised by: Hong Kong Society for Emergency Medicine & Surgery, Hong Kong College of Emergency Medicine & Hong Kong Emergency Nurses Association # HKAM Jockey Club Building Enquiry: Ms. Lenora YUNG & Ms. Jessie CHOW Tel: 2871 8841 Fax: 2871 8898
20-23/10/2006	The First Asian Pacific Symposium on Advanced Molecular Technologies Organised by: Hong Kong Society for Molecular Diagnostic Sciences Ltd, The Hong Kong Polytechnic University (Department of Health Technology and Informatics) & Chinese American Association for Clinical Microbiology Chairman: Dr. TAM Chuen Chu Speaker: Various # The Hong Kong Polytechnic University Enquiry: Mr. HUI Wai Ting Tel: 9464 7392
5-9/11/2006	7th Asian Congress on Oral and Maxillofacial Surgery Hong Kong Organised by: Hong Kong Association of Oral and Maxillofacial Surgeons Ltd Chairman: Prof. Nabil SAMMAN Speaker: International Speakers # Hong Kong Convention and Exhibition Centre Enquiry: Mr. Daniel CHOK Tel: 2871 8896 Fax: 2871 8898
11-12/11/2006	HKOA Annual Congress 2006 - Knee Surgery 2006: In Pursuit of Excellence Organised by: Hong Kong Orthopaedic Association Chairman: Dr. Wilson LI & Dr. W.M. TANG Speaker: Prof. L ENGBRETTSEN, Prof. A.B. IMHOFF & Prof. W.J. MALONEY # Cyberport Convention & Exhibition Centre Enquiry: Ms. Terry LEUNG Tel: 2632 3482 Fax: 2647 7432 Email: congress@hkoa.org
15-17/11/2006	13th Hong Kong International Cancer Congress & 3rd Annual Meeting of Centre for Cancer Research Organised by: Department of Surgery, University of Hong Kong Medical Centre, Queen Mary Hospital # Cheung Kung Hai Conference Centre, William MW Mong Block, Li Ka Shing Faculty of Medicine, The University of Hong Kong, 21 Sassoon Road, Pokfulam, Hong Kong Enquiry: Congress Secretariat Tel: 2855 4235 Fax: 2818 1186 Email: hkjcc06@hku.hk Website: www.hkicc.org
1-3/12/2006	9th International Symposium on Thrombolysis and Acute Stroke Therapy (TAST 2006) & 19th Annual Scientific Meeting of The Hong Kong Neurological Society Organised by: The Hong Kong Neurological Society, Chinese Society of Neurology & The Hong Kong Polytechnic University (Rehabilitation Science Department) Speaker: Various # Jockey Club Auditorium, The Hong Kong Polytechnic University Enquiry: Conference Secretariat Email: tast2006@icc.com.hk Website: www.tast2006.com
8-10/12/2006	Asia Pacific EBM Network Conference "Constraints and Solutions" 8-10 December 2006 Venue: School of Public Health, PWH Conference Secretariat Email: hkcochrane@cuhk.edu.hk Tel: 2252 8710 Website: http://www.hkcochrane.cuhk.edu.hk



Meetings

25-27/01/2007	International Colorectal Disease Symposium (ICDS) 2007 Organised by: Hong Kong Society for Coloproctology & Pamela Youde Nethersole Eastern Hospital (Department of Surgery) Chairman: Mr. Michael K.W. LI Speaker: Various # 2/F New Wing, Hong Kong Convention & Exhibition Centre Enquiry: Ms. Olivia HO Tel: 2595 6362 Fax: 2515 3195
2-4/02/2007	Cardio Rhythm 2007 Organised by: Hong Kong College of Cardiology & Chinese Society of Pacing and Electrophysiology # Hong Kong Convention & Exhibition Centre Enquiry: Secretariat, CMP Medica Pacific Limited Tel: 2559 5888 Fax: 2559 6910 Email: info@cardiorhythm.com Website: www.cardiorhythm.com
13-17/06/2007	The 21st Congress of International Association of Paediatric Dentistry IAPD Organised by: Hong Kong Society of Paediatric Dentistry # Hong Kong Convention & Exhibition Centre Enquiry: Mr. Daniel CHOK Tel: 2871 8896 Fax: 2871 8898 Email: info@iapd2007.com Website: http://www.iapd2007.com

Courses

2/10/2006 - 08/01/07	Certificate Course for Development of Advanced Nursing Practice Organised by: College of Nursing, Hong Kong Enquiry: Sugar Tel: 2572 9255 Fax: 2838 6280
2-12/10/2006 & 6/11/2006 - 14/12/2006	家務助理陪月服務訓練課程 (TC-PNC-0106 & TC-PNC-0206) Organised by: College of Nursing, Hong Kong Enquiry: Sugar Tel: 2572 9255 Fax: 2838 6280
4/10/2006 - 8/11/2006	保健員深造課程〈藥物學〉(TC-AHW-0106) Organised by: College of Nursing, Hong Kong Enquiry: Sugar Tel: 2572 9255 Fax: 2838 6280
4/10/2006	Post-Registration Certificate Course in Intensive Care Nursing Organised by: Institute of Advanced Nursing Studies Enquiry: Course Secretariat, Institute of Advanced Nursing Studies, Hospital Authority, Queen Mary Hospital Tel: 2855 5836
4/10/2006	Clinical Nurse Specialist Group Evening Forum - Pain Management & Care of Dying Organised by: College of Nursing, Hong Kong Speaker: Ms. Sylvia WONG & Ms. Camila LI Enquiry: Sugar Tel: 2572 9255 Fax: 2838 6280
2/10/2006 - 9/11/2006	醫療護理英語基礎課程 (TC-FEC-0106) Organised by: College of Nursing, Hong Kong Enquiry: Sugar Tel: 2572 9255 Fax: 2838 6280
13/10/2006 - 29/12/2006	Certificate Course on Quality Management (TC-CQM-0106) Organised by: College of Nursing, Hong Kong Enquiry: Sugar Tel: 2572 9255 Fax: 2838 6280
13 & 14/10/2006	The Third Annual Training Program, HKSIEP "IEM in Hong Kong - Past, Present and Future" Organised by: Hong Kong Society of Inborn Errors of Metabolism Chairman: Dr. T.S. LAM Speaker: Various Enquiry: Dr. WONG Kar Yin Tel: 7306 9532 Fax: 2855 3334
10&17/12/2006	Pre-hospital Trauma Life Support (PHTLS) Provider Course Organised by: Department of Surgery, University of Hong Kong and Hong Kong Chapter of the American College of Surgeons Enquiry: Course Secretariat, Department of Surgery, University of Hong Kong Medical Centre Tel: 2530 8016