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Optimising the use of oral antibiotics in acne

Speaker: Prof. Brigitte Dréno
Department of Dermatology, Nantes University Hospital, France

Many different drugs are available for the treatment of acne vulgaris. These include oral and topical antibiotics, topical benzoyl peroxide, topical retinoids, oral isotretinoin, oral anti-androgens and zinc salts. Among these, systemic antibiotics is frequently prescribed as *Propionibacterium acne* plays an important role in the pathogenesis of acne vulgaris. Many guidelines were developed for the optimal use of different agents but there is no clear consensus or guideline on the prescription of oral antibiotics such as the dose and duration. Bacterial resistance to antibiotics has become a major problem in the treatment of acne vulgaris as a result of inappropriate use of antibiotics. These include prescription of antibiotics for excessively long period of time and simultaneous use of more than one antibiotic.

The speaker had performed review of all the publications in Medline and Cochrane review between 1975 and 2003 and made the following recommendations to facilitate the daily practice of physicians. Firstly, cyclines should be used in preference to other classes of antibiotics because of their relatively high efficacy, safety and lower antibiotics resistance. Among different cyclines, second generation cyclines should be used in preference to first generation cyclines as they have better pharmacokinetics advantages. Lymecycline and doxycycline have better side effect profiles and should be used in preference to minocycline. The final choice will, however, depend on the patient characteristics, season, UV exposure and country. Secondly, cyclines should be prescribed at high dose to reduce the chance of development of resistance. Lymecycline 300 to 600 mg daily, minocycline and doxycycline 100 to 200 mg daily, tetracycline and oxytetracycline 1 g daily are all effective regimens. Thirdly, there is no evidence that additional benefit can be obtained by antibiotic prescription for more than three months. Fourthly, oral antibiotics should be combined with topical retinoid as these will target different pathophysiologic factors of acne. Finally, topical retinoid should be the treatment of choice for maintenance therapy of acne.

Learning points:

The appropriate use of antibiotics in treatment of acne can result in better efficacy with lower chance of development of bacterial resistance. Recommended guidelines included the use of cyclines at high dose for a period of three months, combination with topical retinoid or topical benzoyl peroxide, and maintenance therapy with topical retinoid instead of systemic antibiotics.

Atopic dermatitis: from pathogenesis to prevention

Speaker: Dr. Richard Langley
Assistant Professor, Division of Dermatology, Department of Medicine, Dalhousie University, Canada

Atopic dermatitis (AD) usually has its onset during the first six months of life. It is frequently the first manifestation of the 'atopic march', with up to 80% of children eventually developing asthma and allergic rhinitis. The exact aetiology of AD is unknown. Genetic, environmental, immunological and skin barrier factors seem to play important roles. The pathogenesis of AD involves the interplay between inflammatory cells such as T lymphocytes, Langerhans' cells, basophils, keratinocytes and inflammatory cytokines such as interleukin-4, 5, 13, 16, and histamine.

Based on the understanding of AD pathogenesis, novel treatment can be developed to inhibit key steps in such process. Calcineurin inhibitors such as pimecrolimus and tacrolimus can inhibit inflammatory cytokines in skin and can inhibit the anti-IgE-induced release of histamine from mast cells. There were studies which indicated that calcineurin inhibitors were effective in controlling acute AD. In addition, flare control and preventing the progression of the atopic march have become two important objectives in the long term management of AD. Pimecrolimus has been shown to prevent AD flare in up to 68% of paediatric patients. To determine whether 1% pimecrolimus cream can prevent the progression of the atopic march, a randomised, multicentre, double-blind, 3-year study with a further 3-year open-label extension, in 1100 infants is currently in progress.

The speaker also mentioned the possible use of topical immunomodulators in other skin disorders such as psoriasis, vitiligo, seborrhoeic dermatitis, perioral dermatitis, contact dermatitis, pyoderma gangrenosum, lichen planus, and graft-vs-host disease.

Newer biological agents which act on IgE and interleukin-5 are also being studied to determine their possible role in the management of AD.

Learning points:

With the understanding of AD pathogenesis, new treatment modalities can be developed. Calcineurin inhibitors such as pimecrolimus are effective in treating acute AD and reducing AD flares. Further evidence is needed to determine whether it can prevent the progression of the 'atopic march'.

Autologous epidermal grafting for treating stable vitiligo: how I do it?

Speaker: Dr. William YM Tang
Social Hygiene Service, Department of Health, Hong Kong

Vitiligo is an idiopathic depigmenting condition characterised histologically by loss of melanocytes in the affected area. Postulated pathogenesis of vitiligo includes autoimmune destruction of melanocytes, self-destruction of melanocytes by toxic metabolite accumulation, neural theory, defects in melanocyte growth factor and genetic susceptibility. Topical steroid and psoralen plus light therapy are effective for vitiligo but some patients fail to respond to these treatments. Autologous epidermal grafting is an alternative for a subgroup of refractory vitiligo patients. Careful case selection is important. The potential candidate should have stable vitiligo, i.e. stable in size, no new vitiligo lesion and no Koebner phenomenon for two years. He should also be motivated, mature, co-operative and the lesion site should be in an area of cosmetic concern. Prior consent has to be taken after full explanation of the procedure, including the risk of Koebnerisation. The process entails collection of the graft from the donor site, preparation of the recipient area, and finally placement of the graft onto the recipient site.

Choice of donor site is important. It should be flat, non-hairy and preferably at areas with thin epidermis. One of the favourite sites is the inner arm. There are a number of ways in which skin graft can be collected, ranging from punch graft, split thickness skin graft to more sophisticated methods requiring laboratory support such as melanocyte culture and melanocyte-rich keratinocyte culture. The speaker employs suction to harvest epidermis from the donor site. Suction allows easy separation of the epidermis at the dermoepidermal junction without scar formation. A continuous negative suction pressure of 300 mmHg is generated by a machine and is applied to the donor area through suction cups. Well-formed blister can be collected after one to two hours. The roof of a blister is then harvested by using a curved fine scissor with care. Securing the epidermal graft onto a piece of fine gauze can facilitate further manipulation and transfer. The graft-gauze composite is transferred onto a platform. The graft is then spread meticulously to its greatest dimension and any fibrin clot, if present, is removed. The graft-gauze composite is then cut along the graft margin, leaving a small part of 'uncovered' gauze for handling. Before transfer of the skin graft, the epidermis of the recipient site should be removed. After preparation of the recipient site by topical EMLA application, hair removal and disinfection, the speaker uses manual diamond fraise dermabrasion to remove the epidermis. Abrasion can be stopped when the papillary dermis is reached and the prepared graft can then be transferred to the recipient site. Simple dressings for donor and recipient areas are adequate and the grafted areas should be immobilised in the first three days. Antibiotics and analgesics are usually not required. Pigmentation may continue to increase up to six months after grafting and hence adequate follow-up time should be allowed before one can decide on the need for repeating the procedure.

Suction-induced blister epidermal repigmentation is a safe procedure that can be of potential help to vitiligo cases not responding to conventional therapy. There are several disadvantages, including a long procedure time, small coverage area per treatment session, and achromatic fissures requiring further treatment. Further studies may optimise the methods and results of the procedure.

Learning points:

Autologous epidermal grafting can be used in vitiligo cases not responding to conventional treatment. Careful case selection is required to optimise the result. Potential cases should have stable vitiligo in an area of cosmetic concern and are motivated to comply with post-operative care.

Granuloma annulare: review of 31 cases and a case-control study of its association with diabetes mellitus

Speaker: Dr. Po-Tak Chan
Social Hygiene Service, Department of Health, Hong Kong

A clinical study investigating the clinical features of granuloma annulare (GA) in Chinese patients and the association, if any, between GA and diabetes mellitus (DM), was carried out. It comprised a retrospective study of clinical features of GA and a case-control study of its association with DM. GA cases were identified by review of skin biopsy record of the Social Hygiene Service from 1st January 1990 to 31st July 2004. Three age and sex-matched controls were selected for each case. For cases and controls without any history of DM, fasting blood sugar was arranged after obtaining consent and the results were classified according to the criteria proposed in 1997 by the American Diabetes Association.

A total of 31 GA patients agreed to participate in the study. They were most commonly of the localised subtype (67.8%), followed by the generalised subtype (25.8%). Subcutaneous and perforating GA each accounted for 3.2%. A bimodal age of onset was seen in both male and female GA cases and it ranged from two to 81 years. Age of onset in localised GA was significantly lower than that of the generalised subtype. A male-to-female ratio of 1.82:1 was observed. GA lesions were most commonly distributed over the distal extremities. The morphology ranged from predominantly annular, predominantly papular to mixed annular and papular in typical GA. Subcutaneous nodules were present in subcutaneous GA, whereas lesions of perforating GA were umbilicated papules. Except for a minority of patients who reported sunburn, topical herbs, common cold and summer season as aggravating factors, the majority of GA cases (90.3%) did not recall any factors that triggered the onset of lesions. Topical steroid was the most commonly prescribed treatment and 16 cases had complete remission after topical steroid. One case of generalised GA responded to a six-month course of oral isotretinoin. Dapsone had been tried in one case but it failed to clear the lesion and in that case, complete remission was finally achieved by topical and intralesional steroid. The median time for first complete remission of GA lesions was 43 months. The time to first complete remission was not affected by GA types, DM status and age of onset. Of the remitted cases, 33.3% had relapsed after a median time of 9.5 months.

DM was present in 23% of GA cases. In generalised GA, the prevalence of DM was 50% as compared with that of 15% in localised GA. Because of the difficulty in recruiting enough controls, only 22 GA cases were included in the case-control study. This study did not find a significant association between GA and DM. Subgroup comparison of generalised and localised GA with their respective controls also failed to demonstrate a significant DM association.

Learning points:

The majority of GA cases are of the localised subtype. There is no association between GA and DM in the present study.

The impact of environmental factors on skin and related skincare

Speaker: Dr. Tilmann Reuther
Division of Cosmetic Sciences, Department of Chemistry, University of Hamburg, Germany

Ultraviolet (UV) irradiation is the major risk factor for skin ageing. UVA, in particular, penetrates into the dermis and generates free radicals which subsequently degrade collagen fibres and damage elastic tissues.

Another environmental risk factor for skin ageing is cigarette smoking. Either direct (inhalational) or indirect (skin) exposure to cigarette smoke can increase skin surface pH that subsequently alter the physiologic function of stratum corneum. Apart from decreasing elastin (by enhancing matrix metalloproteinase-1), cigarette smoke reduces the biosynthesis of collagen in the dermis.

Air pollution can speed up ageing process. Important pollutants are ozone (O_3), nitrogen dioxide (NO_2) and sulphur dioxide (SO_2). Exposure to ozone depletes antioxidant, oxidizes lipids and proteins within the stratum corneum, proliferates cell nuclear antigen, induces heme oxygenase 1 and cyclooxygenase 2. Equally damaging, nitrogen dioxide reacts with cutaneous amines to form nitrosamines.

Although normal skin has an effective antioxidant system, the antioxidant capacity declines with

increasing age. To prevent premature skin ageing, sunscreens and antioxidants are used. Examples of topical antioxidants are L-ascorbic acid (vitamin C), alpha-tocopherol (vitamin E), coenzyme Q10 and flavonoids. Nevertheless, to be effective, they have to be applied at a sufficient concentration, stable in the formulation, and readily absorbed into the skin.

Learning points:
A combination of broad spectrum sunscreens and antioxidants can help preventing premature skin aging. The concentration, stability and ease of absorption of the topical oxidant in the formulation will affect its protective effect.

Laser in dermatological surgical treatment of skin diseases

Speaker: Taro Kono
Chief of Laser Unit, Department of Plastic and Reconstructive Surgery, Tokyo Women's Medical University, Japan

The theory of selective photothermolysis by Dr. Anderson and Dr. Parrish has made it possible to develop short-pulsed, pigment-specific lasers in the treatment of a wide variety of pigmentary skin diseases with a high degree of tissue selectivity and a low risk of post-operative complications. Lasers have been used in the treatment of vascular lesions, hair removal and pigmented lesions.

Long pulsed vascular lasers have several advantages. Firstly, a wavelength of 595 nm is well absorbed by haemoglobin but is less absorbed by melanin. It also has a greater depth of penetration. Secondly, a pulse duration ranging from 1.5 to 40 msec covers the thermal relaxation time of small to large vessels. In conjunction with cryogen spray cooling, long pulsed vascular lasers can be safely used at a higher fluence in the treatment of vascular lesions. They have been used in the therapy of portwine stain, infantile haemangioma, telangiectasia and leg veins. The speaker reports further improvement with long pulsed vascular lasers in cases of residual portwine stain that have already been treated by traditional lasers. In infantile haemangiomas, the use of long pulsed dye lasers together with cooling devices clears lesion significantly faster than traditional vascular lasers. Although hypopigmentation and hyperpigmentation can occur after the procedure, scarring is absent. Long pulsed vascular lasers with cooling device have also been used in the therapy of leg veins. Side effect of the procedure includes hyperpigmentation, but no hypo-pigmentation or scarring is observed. However, one must note that the procedure is only suitable for small and superficial leg veins. For larger and deep leg veins, surgery or sclerotherapy should be considered.

Q-switched (QS) Ruby, QS Alexandrite and QS 1064 nm Nd:YAG lasers have been used for the treatment of naevus of Ota. In a study on the use of QS Ruby laser in two different age groups (adults and children), the children group had an excellent result in fewer sessions and a lower complication rate than the adult group. But it is also reported that pigmentation of naevus of Ota may recur after complete clearance by laser treatment. Hence the advantages and disadvantages of treating naevus of Ota in early childhood should be discussed with the parents before therapy is given.

In the treatment of naevomelanocytic naevi, a combined laser approach is suggested. Firstly normal mode ruby laser is used to remove the epidermis and in doing so, a greater degree of penetration can be achieved by the second laser, QS Ruby, aiming at nests of melanocytes deeper down in the dermis. The combined laser approach works best for naevi with most of the melanocytes distributed in the superficial dermis. Long term follow-up to look for recurrence and malignant change is also an important aspect in management. Laser has been useful in removal

of some but not all tattoos. Multiple laser machines are required if the tattoo has different colours.

A number of lasers can be used in the treatment of lentigines, which are epidermal pigmented lesions. A study has been performed to look into the difference between QS 532 nm Nd:YAG laser and long pulse 532 nm Nd:YAG laser in the treatment of lentigines. Long pulse laser works through its photothermal effect, whereas QS laser has both photothermal and photomechanical effects on the target chromophore. It is observed that long pulse laser has a lower risk of postinflammatory hyperpigmentation and hence the photomechanical effect of QS laser may be undesirable in the treatment of lentigines. The main concern regarding the use of long pulse laser is the potential of thermal diffusion from the epidermis to the dermis and thereby increasing in risk of scar formation. To prevent such complication, the pulse duration should be shorter than the thermal relaxation time of the epidermal basal layer.

Learning points:

Selection of appropriate lasers is important in the management of pigmentary skin diseases. Further improvement in outcome can be achieved by refinement of laser characteristics and cooling devices.

Recent update in sexually transmitted infections

Speaker: Dr Michael KT Chan
Special Preventive Programme, Centre for Health Protection, Department of Health, Hong Kong

Sexually transmitted infections (STI) are major health problems worldwide. Apart from being a substantial burden to the community, they facilitate HIV transmission. The speaker updated the management of various STI.

Molecular testing of *Treponema pallidum* gene sequence has been promising. Based on the fact that each *T. pallidum* strain carries a unique tprK gene sequence, this molecular technique can differentiate relapse from reinfection. Relapse is more likely if the gene sequences of two consecutive infections are similar. Azithromycin is a new alternative treatment for syphilis. A single oral dose of azithromycin is a cost-effective treatment for incubating syphilis, when the standard intramuscular therapy is not feasible. However, it should be used with caution in HIV-infected persons. Single dose azithromycin is also used as syphilis prophylaxis for men who have sex with men (either incarcerated or in the community) or core transmitters of STI.

Based on the type-specific glycoprotein G2, herpes simplex type-specific antibody assay has high sensitivity (80-98%) and specificity (>98%). This assay is used as a behavioural surrogate marker or to diagnose unrecognised herpes simplex infection.

The use of nucleic acid amplication tests (NAAT) becomes the modern paradigm for confirming infection of Neisseria gonorrhoeae or *chlamydia trachomatis*. In suspected gonorrhoea infection, the genital secretion is used for DNA hybridisation and polymerase chain reaction (PCR) while the urine specimen is used for ligase chain reaction (LCR). Similarly, nuclei acid hybridisation, PCR and LCR are used to confirm *chlamydia trachomatis* infection. Although the sensitivity of these tests varies from 50% to 95%, the specificity is as high as 95-99%.

Learning points:

Recent advances in the testing, treatment and prevention of STI give health care providers better opportunities in delivering quality care to their patients.

Radiofrequency, light-emitted diode, fractional resurfacing and laser/light source for fat reduction

Speaker: Dr. Henry HL Chan
Associate Professor and Chief of Dermatology University Department of Medicine, The University of Hong Kong, Hong Kong

Unipolar radiofrequency (RF) has recently been introduced for non-ablative skin rejunvenation in dark-skinned patients. Such technique involves passage of electric current into the tissue with cooling to protect the epidermis. Bulk heating is generated due to tissue resistance to the electric current. This then leads to collagen contraction and shrinkage. This application is now US FDA approved for the treatment of periorbital wrinkling and has been introduced in Hong Kong since November 2003. The speaker claimed good results were achieved with this technique in his study. Bipolar RF in combination with intense pulsed light (IPL) has also been used in skin rejunvenation and appears to be as effective as IPL in term of pigment reduction. However, there is a lack of data in supporting the use of such combination rather than IPL alone. In comparison to bipolar RF, unipolar RF can penetrate deeper than bipolar RF. Complications of RF treatment include burn, numbness, pigmentation, fat indentation and tissue irregularity. New treatment guidelines to reduce the chance of such complications have been developed. These included the use of multiple passes at lower energy setting, avoidance of fat pad, use of the vector approach, and adoption of immediate tissue tightening as end-point.

Laser tissue interaction can be photomechanical, photothermal, and photochemical. Photomodulation is the use of low energy laser to alter cellular function. Light-emitting diode (LED) laser is a recent development which was shown to be effective in offsetting acute sunburn. This finding suggests that LED may be beneficial in the reduction of postinflammatory hyperpigmentation after laser or IPL therapy.

Fractional resurfacing (FR) is a new technique which involves the use of a 1540 nm laser to create microscopic spots of thermal injury. Its aim is to obtain laser resurfacing result with minimal down time. No post-treatment bleaching agents and sun protection are needed. The problems with FR are pain during the procedure and post-treatment erythema and bronze discoloration. Only several dark-skinned patients were treated with this device. Preliminary data indicated that post-inflammatory hyperpigmentation did not appear to be an issue. Further large-scale study looking at its use in the treatment of photoaging in dark-skinned patients is necessary.

Laser and broad spectrum light source have been used to treat cellulite. Preliminary data suggested that they could increase localised metabolism of fat, reduce localised oedema and improve lymphatic drainage.

Learning points:

Radiofrequency, light-emitting diode laser, and fractional resurfacing are new techniques in the treatment of photoaging. Further large scale studies are needed to support their use in the Chinese population.

Update in HIV management

Speaker: Dr. Kenny CW Chan
Kowloon Bay Integrated Treatment Centre, Department of Health, Hong Kong

Highly active antiretroviral therapy (HAART) is the standard of care for HIV infection. The Hong Kong Scientific Committee on AIDS adopts it as the treatment of choice in HIV infection because its use in the local settings has resulted in decreased mortality.

HAART can be defined as combination therapies that potently suppress the viral replication in a durable fashion. Traditionally, it consists of a backbone of two nucleoside reverse transcriptase inhibitors (NRTIs) and a protease inhibitor (PI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI). For those patients who are unable to tolerate these traditional regimens as in the case of significant lactic acidosis or multiple resistances, non-NRTI-containing regimen is a viable option.

It is now clear that different HAART regimens have different degrees of potency in viral suppression. Superiority is emerging for certain antiretroviral drugs or regimens. Kaletra (ritonavir-boosted lopinavir) is regarded as the preferred protease inhibitor by the US authority and the British HIV Association because of its potency, durability and high genetic barrier. Its superiority is supported by well-conducted clinical trials. On the other hand, the use of certain triple-nucleoside therapy (such as abacavir/tenofovir/lamivudine) results in early treatment failure and should be used with caution due to a lack of potency, emergence of K65R mutation (secondary to tenofovir or abacavir) and M184 V mutation (secondary to lamivudine).

Therapeutic drug monitoring (TDM) is perhaps a new breakthrough in HIV medicine. Although TDM for selected antiretroviral drugs (such as indinavir and nelfinavir) was studied, its clinical use has been questioned. Firstly, meaningful reference values are lacking. Secondly, the measurement of intracellular drug concentration is difficult. Thirdly, optimal sampling strategy is not well defined. In the US, TDM is indicated when there is potential drug-drug interaction. In situations where impaired drug absorption is suspected or the patient has narrow therapeutic window (such as pregnancy), TDM is theoretically useful in guiding the physicians to achieve the optimal concentration.

Lipodystrophy is one of the major morbidities in HIV-infected patients. Previous treatment options were facelift and fat grafting. While facelift is a difficult procedure, fat grafting is limited by the paucity of fat in lipodystrophic patients. The novel treatment is facial implant with permanent or temporary injectable dermal filler. Nevertheless, the permanent filler may be complicated by the risk of allergy, dislocation, granuloma formation and irrecoverable technical errors. The temporary filler needs to be injected at regular intervals as it is absorbed within 3 to 6 months. Poly-L-lactic acid is one of the temporary fillers that demonstrate promising result.

Learning points:

HAART is the standard of care for HIV infection. Superiority (and inferiority) is emerging for certain antiretroviral drugs and regimens. Therapeutic drug monitoring is on the horizon.