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Therapeutic update in paediatric dermatology

Speaker: Professor Seth Orlow
 Chairman, Department of Dermatology, New York University School of Medicine, USA

1. Haemangioma

Childhood cutaneous haemangioma has always been a therapeutic challenge. A case report of two infants showed that topical 5% imiquimod three times per week was able to promote substantial regression. Another study of 10 infants showed that more aggressive imiquimod therapy of five times per week and treatment period up to 16 weeks was also effective. Ulcerated haemangioma usually has rapid growth phase and occurs at perigenital or periorificial area. Local measures include topical antibiotics for infection, skin barrier cream and anaesthetic cream for symptomatic relief. Systemic and intralesional corticosteroid were effective in arrest growth and promote regression. Pulsed-dye laser was also an effective modality of treatment. New topical treatment with Becaplermin gel 0.01% (recombinant human platelet derived growth factor) once daily with dressing and barrier cream was shown to promote healing of ulceration in three to 21 days.

2. Intravenous immunoglobulin (IVIg) for childhood Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)

A recent study of 35 children treated with IVIg for SJS and TEN, started at an average of 2.7 days after onset, with an average dose of 2.0 g/kg/day showed cessation of blistering in two days. The efficacy was better with longer duration of therapy of three to four days when compared to duration of less than three days. The main adverse event was decrease in white cell count, but was reversible when treatment was stopped.

3. Molluscum contagiosum

In a double-blind randomized pilot trial of molluscum contagiosum, 23 children of age one to nine year, were randomized to receive 5% imiquimod topically or vehicle three times per week for 12 weeks. Partial clearance (> or =30% clearance) were shown in 58% (7/12) at week 4 and 67% (8/12) at week 12 for patients receiving imiquimod. However, partial clearance was none (0/11) at week 4 and 18% (2/11) at week 12 in the vehicle group. Complete clearance was attained by 33% (4/12) of imiquimod patients at week 12. The treatment was well tolerated.

4. Pediculosis capitis

Pediculosis capitis causes significant morbidity in terms of loss of school and working days. It sometimes shows resistance to the usual topical treatments. The therapy of oral Thiabendazole 20 mg/kg for one dose and repeated 10 days after first dose only shows fair result. A dry-on suffocation based therapy with Cetaphil lotion was effective in an open clinical trial. Water soluble

Cetaphil lotion is a non-toxic lotion composed of stearyl alcohol, propylene glycol, sodium lauryl sulfate, acetyl alcohol, water, methyl-4-hydroxybenzoate, propyl p-hydroxybenzoate and butyl p-hydroxybenzoate. The lotion was applied wet thoroughly and wait for two minutes. The lotion was combed out followed by blow-dry of hair, followed by the use of child's usual shampoo eight hours later. Patient was instructed to either remove nits or leave the nits behind. The lotion was applied once weekly until cure, up to a maximum of three applications. The film layer completely covers the louse and causes death by suffocation. In the trial of 133 subjects, the overall cure rate was 96% and a remission rate of 94% at six months. There was no adverse effect.

5. Vitiligo

Topical tacrolimus was shown to be effective in treating vitiligo. The onset of therapeutic efficacy was usually 11-14 weeks. The best response was observed in those with segmental lesion. Topical tacrolimus was as effective as topical clobetasol propionate to induce repigmentation in a study. However, topical tacrolimus was better tolerated and had better response for facial lesions.

6. Pityriasis rosea

Double-blind placebo-controlled trials showed that oral erythromycin for two weeks was effective to induce resolution of eruptions when compared with placebo. The probable mechanism was the anti-inflammatory action of erythromycin. However, another study showed that azithromycin did not alter the course of the disease.

7. FDA action impact on paediatric dermatology

The treatment of atopic eczema has been advancing with the introduction of calcineurin inhibitors. Pimecrolimus and tacrolimus are the two topical agents approved for use in childhood atopic eczema. There were revised indications for their use, namely as a second line therapy, in area where other topical agents such as corticosteroid were inappropriate, use in child older than two years old, for short term and non-continuous treatment.

Learning points:

There are many new advances in the treatment of various paediatric dermatological diseases. Better therapeutic options are available for previous challenging diseases such as childhood haemangioma, SJS and TEN.

Approach to infantile and juvenile acne

Speaker: Dr. Chi-keung Yeung

Honorary Clinical Assistant Professor, Department of Medicine, The University of Hong Kong, Hong Kong

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit affecting mostly adolescents. Its severity varies from mild to a very distressing and socially disabling disorder. Comedones may precede the development of inflammatory lesions by up to two years and their early onset is the best predictor of future severe acne. The psychosocial impact of acne is often under-estimated and is not always proportional to the physical severity. It is associated with low self-esteem, anxiety, depression, poor interpersonal skills and suicidal ideation in adolescence. Early recognition and therapy may prevent scarring and psychosocial stress.

Neonatal and infantile acne are differentiated by the age of onset and clinical features. Neonatal acne, also known as cephalic pustulosis, often appears in the first few weeks of life as erythematous papulo-pustules without comedones on the face and scalp. It is self-limiting or usually responds to topical antifungals as inflammatory reaction to *Malassezia* species has been proposed to be an aetiology factor. Infantile acne typically occurs in males at around six months of age and presents with comedones, inflammatory papules and rarely nodules that may lead to pitted scarring. The lesions are primarily found on the cheeks and are considered to be driven by androgen. Naevoid acne are an uncommon variant that presents initially as localized linear comedonal lesions at an early age, followed by inflammatory lesions at puberty.

Acne may also be secondary to endocrinologic abnormalitis involving hyperandrogenism, especially between the age of three and seven years. Suspicious features include irregular menstrual periods, hirsutism, obesity, alopecia and poor treatment response. Screening with bone age and growth charts is useful.

Acne fulminans is an acute ulcerative form of acne associated with systemic symptoms. It is sometimes triggered by the use of oral isotretinoin. Treatment involves a tapering course of systemic steroid followed by gradual introduction of oral isotretinoin.

The principles of paediatric acne treatment are the same as for adults. The choice of acne therapy depends on the assessment of physical severity, lesion types and psychosocial effects. Truncal acne, hyperpigmentation and scarring are sometimes overlooked. Compliance is the major issue in acne management in children and adolescents. Adequate discussion with the parents about the chronic nature of disease, side effects of treatment and expected slow response are essential in optimising treatment outcome.

Topical retinoids are used for mild comedonal acne. Treatment of mild to moderate inflammatory disease involves topical benzoyl peroxide, topical or oral antimicrobials and topical retinoids. In children, oral erythromycin is used while oral tetracycline is contraindicated because of the side effect of permanent tooth staining.

Oral isotretinoin is indicated for scarring nodulocystic acne, acne refractory to other treatment or associated with significant psychosocial complications. A minority of patients may develop an acute flare in the first two months of isotretinoin treatment and may require systemic steroid or reduction of isotretinoin dose. Long term adverse effects are infrequent. Adverse skeletal effects are very rare at typical doses (0.5-1.5 mg/kg/day). Monitoring should involve baseline and regular liver function tests and serum lipids as well as bone studies. Pregnancy prevention program guidelines should be strictly followed.

Learning points:

Early recognition and treatment of acne is important to avoid significant physical and psychosocial scarring. Early onset of comedones is the best predictor of future acne severity. Careful education and discussion with parents about acne, the side effects and expected response is essential in management. Oral isotretinoin can be safely used in children for refractory, scarring nodulocystic acne but requires careful monitoring.

Laser treatment of skin diseases in children

Speaker: Dr. Henry Hin-lee Chan

Honorary Clinical Associate Professor, Department of Medicine, The University of Hong Kong & The Chinese University of Hong Kong, Hong Kong

Laser and intense pulsed light can be employed in the treatment of congenital lesions including naevus of Ota, café au lait patch, congenital melanocytic naevi, port wine stain, and proliferative haemangioma. These therapies can also be used to treat vitiligo.

However, the use of laser therapy in congenital melanocytic nevi in Asian is controversial because of the concern of potential neoplastic change. Ruby laser with longer pulse duration achieves better result than Q-switched laser. For naevus of Ota, Q-switched ruby laser achieves better result in younger age group and complication rate is lower. Epidermis in children is thinner in comparison with adult so that laser has better penetration and reaches nevomelanocytic cells more easily. The risk of recurrence is 0.6-1.2%. For café au lait patch, Q-switched laser has demonstrated variable result and frequent recurrence.

Laser and light therapy can also be used to treat vascular lesions like port wine stain, haemangioma and scar. Pulsed dye laser is the

laser of choice in port wine stain due to its lower risk of scarring, less pigmentary change and relatively higher rate of clearing. The addition of a dynamic cryogen cooling device has advanced the treatment by epidermal protection via surface cooling and selective heat accumulation in vessels. Children with port wine stain should be treated early to prevent adversity on their psychological development. The use of laser therapy in proliferative haemangioma is debatable. Ulceration has been reported in patients with haemangioma treated with pulsed dye laser. Traditional pulsed dye laser with shorter pulse duration has more complications than pulsed dye laser with longer pulse duration. The use of laser therapy in scar is notably very effective.

Photodynamic therapy by combination of topical photosensitizer and deep penetrating broad band red light can be used to treat acne and cause shrinking of sebaceous gland. The side effects are crusting, exfoliation and pigment change.

Learning points:

Judicious use of laser and intense pulsed light source has advanced treatment for congenital skin lesions in paediatric population.

Skin manifestations in primary immunodeficiencies

Speaker: Professor Yu-lung Lau

Chair Professor & Head, Department of Paediatrics & Adolescent Medicine, The University of Hong Kong

There are currently over 100 types of primary immunodeficiencies with defined genetic defects. Their clinical presentations are widely variable. More than 40% of them have a deficiency predominantly of the humoral immunity. It is important to have an early and accurate diagnosis, so that optimal treatment, genetic

counselling and prenatal diagnosis can be offered to avoid or minimize long term complications.

Making an accurate diagnosis starts with a good history and clinical examination, together with blood tests for screening. They include absolute neutrophil count (ANC), absolute lymphocyte count (ALC), platelet count and immunoglobulin level. As a dermatologist, one should suspect possible primary immunodeficiencies if patients present with certain skin conditions which appear to be persistent and resistant to conventional treatment, such as refractory eczema, persistent skin and mucosal candidiasis, poor wound healing, cutaneous BCG site infection, hypohidrosis, ecythema gangrenosum, pyoderma, cutaneous lymphoma, urticaria and cystic acne.

Refractory eczema can be a manifestation of Wiskott-Aldrich syndrome (WAS), hyper-IgE syndrome, IPEX (immune dysregulation, polyendocrinopathy, enteropathy, X-linked) and IgG subclass deficiency. WAS presents with petechiae, intracerebral haemorrhage and bloody diarrhoea. It is characterized by small volume platelets and a low platelet count. Hyper IgE syndrome presents with multiple cold abscesses and delayed dentition. IPEX is a recently described condition seen in male infants. It is due to mutation in FOXP3 gene on the X chromosome leading to defective regulatory and effector T-cell function. IPEX patients can present with failure to thrive and diarrhoea, and they can have associated diabetes mellitus, autoimmune enteropathy, haemolytic anaemia and thyroid function abnormalities.

Persistent skin and mucosal candidiasis should alert one to the possibility of severe combined immunodeficiency (SCID) and chronic mucocutaneous candidiasis (CMC). SCID patients can present with failure to thrive and chronic diarrhoea; whereas skin manifestations of CMC can consist of severe nail dystrophy, macroglossia and creased tongue. Cutaneous BCG infection is suggestive of T-cell deficiency. It can be seen in SCID, DiGeorge syndrome and chronic granulomatous disease (CGD). Poor wound healing, late cord separation and chronic gingivitis

can be due to leucocyte adhesion deficiency. Hypohidrosis, hypodontia, conical teeth, periorbital wrinkling and sparse hair in a boy should alert one to X-linked hypohidrotic ectodermal dysplasia. Pyoderma and furuncle can be a feature of common variable immunodeficiency (CVID) and X-linked agammaglobulinaemia. Erythema gangrenosum with neutropenia and mouth ulcer should raise the possibility of severe congenital neutropenia. Urticaria presenting in the first week of life with increased intracranial pressure and cerebral vasculitis are features of chronic infantile neurologic cutaneous and articular syndrome (CINCA). Cystic acne with pyogenic arthritis and pyoderma gangrenosum together are features of 'pyogenic arthritis, pyoderma gangrenosum and acne (PAPA)' syndrome. It is an autosomal dominant condition in which the genetic defect leads to dysregulation of the inflammatory pathway.

It is now possible to offer molecular diagnosis for about 20 different primary immunodeficiency conditions. As dermatologists, it is important to be aware of these conditions so that an early and accurate diagnosis can be made in order to prevent any irreparable organ damage.

Learning points:

Primary immunodeficiencies can present to dermatologists with a variety of skin manifestations. It is important to be aware of these conditions so that an early and accurate diagnosis can be made.

Genetic basis of selected skin diseases

Speaker: Dr. Stephen Tak-sum Lam
Consultant Clinical Geneticist & Head, Clinical Genetic Service, Department of Health, Hong Kong

Genetic disorders can be classified into mendelian inheritance, chromosomal derangements or multifactorial in origin.

Of mendelian inheritance, these single gene disorders can be further divided into autosomal dominant, autosomal recessive and X-linked dominant or recessive. Recently, a number of genetic mutations have been identified for specific skin diseases in this monogenic manner. Single gene disorders are found in the disorders of epidermis in the form of abnormalities of pigmentation (including oculocutaneous and ocular albinism or more localized hypopigmentation disorders in the form of piebaldism and Waardenburg syndrome); keratinization defects in the form of ichthyosiform dermatoses; epidermal adhesion defects in the form of epidermolysis bullosa and ectodermal dysplasia. Furthermore, monogenic inheritance is implicated in other heterogeneous disorders including, Hailey-Hailey disease and trichothiodystrophy, skin malignancies and genetically determined benign tumours. Hereditary disorders of the dermis may be found in the form of connective tissue disorders such as Marfan syndrome, Ehler-Danlos syndrome or elastic tissue disorders such as cutis laxa. Molecular genetic diagnosis is now available for some of the skin conditions.

For chromosomopathies, certain skin features are found to be associated with specific syndromes. These syndromes may be identified by features other than in the skin. For multifactorial conditions, single or multiple genes interacting with the environmental effects may be involved. Common conditions including psoriasis and eczema are intensively studied for their genetic basis and gene-environmental interactions.

Learning points:

Genetic disorders are found in a number of skin diseases. Molecular genetic diagnosis is now available for some of these conditions.

Recent skin rejuvenation trends using IPL technologies

Speaker: Dr. Kei Negishi

Sub-assistant Professor, Department of Aesthetic Surgery & Medicine, Institute of Aoyama Women's and Natural Medicine, Tokyo Women's Medical University, Japan

There are many different modalities for non-ablative facial rejuvenation. These include light sources, lasers and various radiofrequency devices. In recent years, non-ablative photo-rejuvenation by intense pulsed light (IPL) sources has become popular in Asians. It is particularly efficacious in removing epidermal pigment disorders without causing post-inflammatory hyperpigmentation, in contrast to the traditional pigment lasers. In addition, it has the benefit of improving vascular lesions, overall skin tone and skin texture.

A major concern of IPL facial rejuvenation in Asians is the unmasking of latent melasma that results in hyperpigmentation after the IPL treatments. It is therefore recommended to perform ultraviolet light photography before IPL treatment in order to detect latent melasma. The concept of "IPL-individualized wavelength based parameter setting" is introduced. If latent melasma is detected or for those patients with darker skin, longer wavelength spectrum (>600 nm), lower fluence and adjustments in pulse duration should be used for full face rejuvenation. Individual pigmented lesions such as solar lentigo can subsequently be treated with IPL using hand-piece with smaller spot size, shorter wavelengths and higher fluence. Alternatively a Q-switched pigment laser can be used to treat residual pigment lesions. In addition, topical bleaching agents and sunscreen should always be used before, during and after IPL therapy.

This concept of 'IPL-individualized wavelength based parameter setting' for pigmentation and other skin lesions can maximize the treatment result and minimize the risk of complication.

Learning points:

Caution should be exercised in performing IPL treatments on Asian patients. The risk of unmasking latent melasma can be reduced and darker skin patients can safely be treated by using the concept of IPL-individualized wavelength based parameter setting.

Tricks in out patient minor surgery

Speaker: Dr. Man-kwong Tung

Vice Director, Plastic & Reconstructive Surgery Centre, Hong Kong Sanatorium & Hospital, Hong Kong

Before starting the operation, one should try to build a good rapport with the patient and to take clinical photos. Always corrects patients' wrong concepts and expectations and leads the patients back to reality. Drug history, past medical history and history of poor wound healing are important during history taking. In performing the physical examination, watch out for previous scars and any small skin cancer. Furthermore, psychiatric assessment and evaluation of the patients' expectations about the operations are important.

Good preparation of the patient, the doctor, the nurse and the operation theatre are the vital points for success in performing the minor operations. Doctors should correct patients' nutritional deficiencies, to advise them to stop smoking and give antibiotics cover if needed. The doctors should wear eye glasses to correct their visual acuity if necessary and be familiar with the tension lines, arteries and nerves of the body parts. Moreover, well trained nurses may help in performing minor operations. In the operation theatre, good lighting, all necessary instruments, diathermy devices and resuscitation trolley should be available. It is also important to follow up the patients after the minor surgery. Nevertheless, it is a good habit to review after the minor surgery to improve the surgical skills in the future.

Learning points:

History taking, physical examination and communication skills are vital for performing minor operations. Good pre-operative preparation of the patient, the doctor, the nurses and operation theatre are also important tricks in out patient minor surgery.

Management of melasma in Singapore

Speaker: Dr. Joyce Lim

Private Dermatologist, Joyce Lim Skin and Laser Clinic, Singapore

Melasma is a common chronic skin disorder occurring in all skin types, and is among the top 10 diagnoses seen in dermatological clinics in Singapore. Melasma often causes significant psychosocial distress and has a wide clinical spectrum: epidermal, dermal or most frequently mixed. In addition, some patients may have very subtle epidermal melasma that may be invisible to the naked eye and can be exacerbated by intense pulsed light (IPL) treatment. Melasma is also frequently associated with acquired bilateral naevus of Ota-like macules (ABNOM) which may be subclinical and unmasked by the treatment for melasma.

Management of melasma is often difficult and involves a combination of sunprotection, removal of any aggravating factors and treatment by topical or light therapies. Treatment has to be tailored to the individual patient and maintenance therapy is often required. In the speaker's experience, some patients may stop producing melasma at a certain age.

Sun avoidance and protection is essential, consisting of the use of broad-spectrum sunscreens, physical ultraviolet light protection and even oral sunblock (fern extract). Other aggravating factors such as oral contraceptive pills, heat and drugs (hydantoin and dilantin) should be avoided.

Specific topical therapies including hydroquinone, tretinoin, azelaic acid, kojic acid and chemical peels can be used. Topical hydroquinone is often used as the first-line treatment and response is usually evident at four to six weeks with maximal response at four to six months. Double or triple combination therapies are usually more effective. Kligman and Willis first described the 'Kligman formula' in 1975, consisting of a combination of topical 0.1% tretinoin, 5.0% hydroquinone, and 0.1% dexamethasone in hydrophilic ointment.

A small study was done in Singapore to assess the efficacy and safety of Tri-luma, a new triple-combination topical agent consisting of hydroquinone 4%, tretinoin 0.05%, fluocinolone acetonide 0.01%, on melasma. Twenty adult Chinese women were enrolled in the study. Tri-luma was applied topically every night for eight weeks and a sunblock in the daytime. Patients were evaluated at four weeks and eight weeks by photographs, mexameter reading and subjective measurements. At the end of the study, none of the patients had complete clearance. The doctor's evaluation showed that seven patients (35%) had minimal melasma while 13 patients (65%) still had obvious melasma. There was no major adverse reactions from the treatment. Interestingly, assessment by mexameter showed reduction of pigmentation at four weeks of treatment, whilst increased pigmentation at eight weeks which may be due to post-inflammatory hyperpigmentation or underlying dermal melasma. In comparison to multi-centre trials, there were higher incidence of side effects of peeling and erythema which may be due to poor tolerance to tretinoin.

Kojic acid is a tyrosinase inhibitor which may be combined with hydroquinone and glycolic acid in the treatment of melasma. Clearance has been reported in 60% of patients using a topical combination gel consisting of 2% kojic acid, 2% hydroquinone and 10% glycolic acid. The lightening effect of azelaic acid 20% cream is comparable to 4% hydroquinone. It may also be used in combination with topical steroid and glycolic acid. Tretinoin 0.1% cream reduces epidermal pigmentation but is commonly associated with

irritant contact dermatitis. Niacinamide inhibits melanosome transfer and is useful if one cannot use hydroquinone or kojic acid agents. The skin lightening effect may occur as early as four weeks.

Chemical peels, IPL, and ablative laser therapies can also be used. IPL has been useful for epidermal melasma but partial repigmentation does occur. Laser therapy (Q-switched Nd-YAG or Fraxel) is useful as a third line treatment of melasma but there is a risk of post-inflammatory hyperpigmentation. Finally, there are currently no evidence available supporting the use of microdermabrasion or antioxidants in the treatment of melasma.

Learning points:

Management of melasma is often difficult and involves sun avoidance, use of daily broad-spectrum sunscreens and exclusion of aggravating factors. First-line treatment involves combination topical agents involving hydroquinone. Chemical peels, IPL and lasers are reserved for refractory cases. Maintenance therapy is often necessary and may include the topical non-hydroquinone agents or tretinoin.

Laboratory diagnosis of viral STI

Speaker: Dr. Janice Yee-chi Lo

Acting Consultant Medical Microbiologist, Microbiology Division, Public Health Laboratory Services Branch, Centre for Health Protection, Department of Health, Hong Kong

In Hong Kong, viruses are one of the major aetiological agents in sexually transmitted infection (STI). Laboratory diagnosis has an important role in the overall management of STI. Common viral STI include human papillomavirus (HPV), herpes simplex virus (HSV), and human immunodeficiency virus (HIV) infection. Chlamydia trachomatis is a bacterial agent commonly diagnosed in the virology laboratory. The epidemiology of STI in descending order are non-gonococcal urethritis/non-specific genital infection (NGU/NSGI), genital

wart, gonorrhoea, syphilis, herpes genitalis, trichomonas vaginalis and human immunodeficiency viral infection according to epidemiology data from Social Hygiene Service in Hong Kong. The laboratory investigations include direct detection of the pathogen or its component, culture and antibody detection by serology.

Direct detection of Chlamydia DNA by polymerase chain reaction (PCR) is suitable for diagnosis and screening in high risk group. Samples can be obtained from male urethra, female endocervix or sometimes urine. Detection of antigen by using direct fluorescent antibody test is a simpler and less expensive method. McCoy cell culture followed by immunofluorescent staining of intracytoplasmic inclusions with monoclonal antibody remains the gold standard in diagnosis and is the only acceptable laboratory evidence in medico-legal cases. It is highly specific in detecting viable organism.

The diagnosis of genital wart is usually clinical. The commonest pathogens are low risk type HPV 6 and 11. Direct DNA detection and probe hybridization in liquid-based cervical cytology specimens form the basis of cervical screening for cervical neoplasm. It is the only FDA-approved method for HPV genotyping but does not differentiate specific types. Type specific PCR is labour-intensive and may be able to detect mixed infection. Generic L1 gene PCR followed by typing restriction fragment length polymorphism (RELP) reversed line-blotting and nucleotide sequencing is an alternate.

Genital herpes are usually caused by HSV type 2 or possibly type 1. Viral culture using Vero cell line is the mainstay of diagnosis and cytopathic effects can be observed as early as day 2 of culture. It can be confirmed by immunofluorescence test. Electron microscopy can be used for direct detection. PCR can yield type-specific result, sometimes superseding viral culture in some centres. Antibody detection has the disadvantage of high degree of cross reaction between HSV-1 & 2 antibody and type specific assays are not widely available. Secondly, result rarely affects

clinical management because culture or direct detection tests are not possible. Presence of antibody does not indicate site of infection. It is important to note that there is no established management protocol for discordant couples. There are also issues with results interpretation and patient counselling.

Antibody detection is the mainstay of laboratory diagnosis to detect both HIV-1 and HIV-2 antibodies. Enzyme immunoassay combing antigen/antibody detection is highly sensitive as screening test and results can be available within hours and positive results require confirmation by Western blot testing and result can be available overnight. RNA detection is licensed for monitoring of viral load for antiviral treatment and may be considered in suspected acute infection.

Learning points:

In diagnosing STI, laboratory support has played an important role. Direct detection of the pathogen or its component, culture and antibody detection by serology are the underlying principles of laboratory investigations. Dermatologists have to pay particular attention to the interpretation of the laboratory results, especially the consideration of false positive and negative results. A careful clinical-pathological correlation is the rule of thumb.

Common pitfalls in the diagnosis and management of STD

Speaker: Dr. King-man Ho

Senior Medical and Health Officer, Fanling Integrated Treatment Centre (Social Hygiene Service), Department of Health, Hong Kong

Commercial Herpes Simplex Virus 2 (HSV-2) type specific antibody test was used as an illustration and different scenarios were discussed. Similar principles could be applied to other sexually transmitted disease (STD) diagnostics such as nucleic amplification tests for Chlamydia and Ureaplasma which are recently introduced in the

market or adopted in places other than Hong Kong.

All laboratory tests cannot fully replace the clinical acumen of the attending physicians. It is essential to determine the objective of ordering the test, to select and interpret these tests in the appropriate clinical context. The test performance indicators, sensitivity and specificity should be noted. These are independent of the pre-test probability but are very sensitive to any deviation from the strictest provisions as incurred from specimen sampling, storage, transport, handling and various steps in the laboratory processing. The figures as specified by the manufacturers may not be reproduced in the actual clinical situations.

It is also important to know the supporting laboratory and the nature of the concerned STD diagnostics. Some tests are approved by reputable regulatory agencies. POCkit and HerpeSelect are examples that are both approved by the Food and Drug Administration of United States while many others are not. The meaning of positive tests should be ascertained. As an example, the term "positive for mycoplasma sp" may not be specific enough to indicate a particular species: ureaplasma urealyticum, mycoplasma genitalium or any of the species. For nucleic amplification test such as polymerase chain reaction or ligase chain reaction for chlamydia or mycoplasma sp., control is required to monitor the presence of inhibitors in the sample. For Elisa Immunoassay tests or tests that involve definition of cut off values to define positivity, it should be checked whether the Receiver Operating Characteristic (ROC) curves are re-defined. It is also important to know whether the laboratory have any quality assurance measures such as detection of the presence of laboratory contamination.

It is essential to interpret the test results in the appropriate clinical context. The positive and negative predictive values are sensitive to the pre-test probability of disease occurrence: the population prevalence in the setting of screening and the clinical acumen of the attending doctor in the setting of diagnostics. The attending doctors have to decide if the index test is applied as a

screening or diagnostic tool. In the setting of clinical diagnostic, the attending doctor has to decide if a positive (or negative) result explains the concurrent clinical presentation or disease of the index case. It is important to remember that the psychosocial impact to the index patient will be even more tremendous compared to his/her physical well being.

A sensitive test with a **negative** result rules **out** the disease (Mnemonic: SnOut) and a **specific** test with a **positive** result rules **in** the disease (Mnemonic: SpPin). It is also important to give a thought for the other combinations e.g. meaning of positive test in a sensitive test; a negative test in a less sensitive diagnostic; and the application of the results in the correct context.

Learning points:

In the use of STD diagnostics, it is essential to have a good appreciation of the clinical context and choose the appropriate test after setting a clear objective of ordering the test. It is also important to know the test performance indicators, sensitivity and specificity, the supporting laboratory and the nature the STD diagnostics. The test results should be interpreted in the appropriate clinical context. The "Axiom Mnemonics" are helpful to remember that a **sensitive** test with a **negative** result rules **out** the disease (SnOut) and a **specific** test with a **positive** result rules **in** the disease (SpPin).