Emerging challenges in Global Health Dermatology

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Nowadays, there are increasing challenges facing internationally-minded dermatologists. Skin conditions were the fourth leading non-fatal causes of disease burden. Cutaneous fungal infection and acne were among the top most common ten diseases in the world in 2010. Collectively, skin conditions account for the 2nd to 11th causes of morbidity at the national level and is of great concern. HIV dermatosis is one of the emerging challenges in Global Health Dermatology. The World Health Organization (WHO) published a guideline on the treatment of skin and oral HIV-associated conditions in children and adults in 2014. Kaposi sarcoma (KS) is one of the major HIV-related dermatosis. It is commonly found in sub-Saharan region in Africa. There was an outbreak of KS in the United States in a group of men who had sex with men (MSM) in 1981-82. Zidovudine (AZT) was not available until 1987 to 1990 and it was used to treat KS. However, the 5-year survival rate was only around 10%. The situation improved drastically after the introduction of highly active antiretroviral therapy (HAART) in around 1996 and by measurement of HIV viral load, and discovery of the causative virus – human herpesvirus 8. The survival has then greatly improved. However, in HIV-infected patients, the presence of KS is associated with a five-time higher mortality compared to those without KS. Although in the era of HAART, KS is still endemic in some areas and causes multiple problems such as GI bleeding, lymphoedema and so on. Moreover, KS can occur even when the CD4 count is high and the viral load is undetectable. As HAART alone may not be adequate for treating KS, chemotherapy like liposomal doxorubicin is commonly used. However, further studies are needed to explore more effective treatment for KS in order to respond to this challenge.

Learning points:
Skin conditions lead to significant morbidity in HIV patients. HIV dermatosis is now becoming increasingly important and the WHO has published guidelines on the treatment of skin and oral HIV-associated conditions in children and adults. Kaposi sarcoma is commonly seen in HIV patients and has a higher mortality than that in HIV-negative cases. HAART is the mainstay of treatment and chemotherapy is needed if there is systemic involvement.
Dermoscopy is useful for early identifying malignant melanoma and improving the diagnostic accuracy of melanoses. It can minimise unnecessary biopsies and removal of benign lesions. It is important to familiarise oneself with the dermoscopic features of both benign and malignant lesions. Basically, the most common patterns in benign melanocytic lesions are:


Moreover, the dermoscopic features of a skin lesion may vary according to the location, age and skin type. Benign melanocytic naevi on the face, trunk and nails may have a different dermoscopic appearance. Naevi with a peripheral globular pattern may decline rapidly after the third decade and no longer be observed in the sixth decade. Melanomas almost invariably display some degree of asymmetrical pattern, colour and structure. They deviate from the global benign pattern and may have the following patterns:


The face is a specific region for dermoscopist because different sites have different dermoscopic appearance and no one would like to have unnecessary biopsy on their faces. A study showed that 87% of 125 cases of lentigo maligna had at least one of the following features:


Therefore, a biopsy should be considered if these features are present.

For non-melanotic lesions, the first step is to identify any melanotic features to exclude a melanotic lesion and then look for any specific features of a particular lesion. Dermatofibroma may present as central scar like white colour and peripheral pigment network. Some may show dotted vessels along the lesion. Basal cell carcinoma may have arborising vessels, maple leaf, blue grey globules or ovoid nest. Seborrhoeic keratosis shows classically multiple milia like cysts and comedone like openings. The speakers concluded that benign features are simple and easy to describe. If the dermoscopic features cannot be described, biopsy the lesion.

Learning points:
Dermoscopy has the advantage of improving the diagnostic accuracy of melanoma by identifying specific features. It can help to reduce unnecessary biopsies especially on the face. However, dermoscopic features may vary with age, location and skin type. A biopsy is still needed to confirm the diagnosis if there are any suspicious features.
Dermatologic surgery disasters: a dissection of patient safety failures

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Patient safety has an integral role in the strategy to improve US health care. Medical errors were detected in 44,000 to 98,000 patients in US hospitals in 2000. Most dermatological surgeries were done in the office-setting. A study found that the safety of office-based surgical procedures done by skilled professionals with proper patient selection was the same as those done in hospitals. Most common diagnoses in malpractice claimed against dermatologists in 1985 to 2006 were malignant neoplasm, acne dyschromia, psoriasis and malignant melanoma. A study found that 11% of US Moh surgeons reported that among the medical lawsuits brought against them in 2006, incorrect operation site was the most common one. Others included infection, post-operation bleeding and medication errors. It has been shown that 5.9% of Mohs surgeons incorrectly identified the biopsy sites using anatomical description on records. In contrast, all biopsy sites could be correctly identified if a clinical photograph was taken. Therefore, the speaker suggested using pre-biopsy photographs to reduce the possibility of incorrect site operation.

Retinal artery occlusion is a known complication of filler injection that can lead to blindness. Excruciating pain and sudden blackout may be the clinical presentation of acute retinal artery occlusion. Central retinal artery embolisation is due to retrograde arterial displacement of injected material from the peripheral vessel into the ophthalmic artery system. Higher injection pressure may even cause retrograde migration of foreign material into the internal carotid artery and subsequently causing cerebral embolisation and stroke. There is still no effective and reliable treatment for retinal artery embolisation. Aspiration before injection, using a smaller size cannula, applying local vasoconstrictor, limiting the volume of filler injected and avoiding injection at previously traumatised tissue may prevent retinal artery embolisation.

Learning points:
Clinical photography is a useful tool to avoid incorrect side and wrong site operation errors. Retinal artery occlusion is a serious adverse effect of filler injection for which there is no effective treatment.

AIDS and Sexually Transmitted Diseases (STDs): hot topics

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HIV skin manifestations are important nowadays as 65% of men who had sex with men (MSM), 20% of intravenous drug users (IVDA) and an increasing number of heterosexual men have HIV infection. Kaposi sarcoma (KS) is an HIV-related dermatosis. KS can manifest on the skin as purplish papules, nodules and even as plaques or patches. The main treatment is combination anti-retroviral therapy (cART).
median time for resolution of KS after cART is around 9 months. Patients with KS have around 4.7 times higher mortality than those without KS in HIV-infected patients. Though KS commonly occurs in patients with a low CD4 count, patients with a high CD4 count and low viral load after cART may still have KS. This is similar to classic KS. Chemotherapy is considered for patients with systemic involvement and those with a high CD4 count. Eosinophilic folliculitis can cause intractable itchiness in patients and is also commonly found in HIV-infected patients especially when the CD4 count is lower than 200/mm³. Itraconazole is the main treatment. Permethrin cream, phototherapy and retinoids can also be used. Viral warts are common and may worsen if CD4 count is low and does not improve even after the initiation of cART. It may increase the risk of malignancy. Anal cancer and dysplasia are commoner in HIV patients and are not improved by cART. Other non-melanoma skin cancers are around two times more common in HIV-infected individuals. Squamous cell carcinoma may be more aggressive and has a higher recurrence rate.

Although cART can promptly reduce the HIV viral load, the virus cannot be eradicated as it is localised mainly in the T cells and in the lymphoid tissue. Hence cART needs to be taken lifelong. As for other medications, the route of administration, toxicities, infrastructure and even the cost of cART should be considered. Besides, cART has its own limitations and adverse effects. The cART cannot fully reverse the disease. It may increase the risk of coronary artery disease, liver and renal failure and even osteoporosis. Therefore, new methods to cure HIV or prevent HIV infection such as vaccination are still under investigation.

Syphilis is a great mimicker. Patients may be co-infected with HIV and syphilis especially in high risk groups. In one study, 20% of 460 MSM had repeated syphilis infection, of which 86% were HIV positive. Apart from syphilis, other STIs such as chlamydia, gonorrhoea should also be screened. The presentation of STI in HIV infected patients may be atypical and more severe. Therefore details in the sexual history and thorough physical examination as well as screening of syphilis are necessary in HIV patients. If the patient is HIV-negative and has high-risk behaviour, pre-exposure prophylaxis (PrEP) may be considered.

**Learning points:**
As HIV and syphilis co-infection can occur, screening for syphilis is important in HIV-infected patients. The presentation of STI may be atypical in HIV patients. A careful and detailed sexual history and physical examination is needed. If the patient is HIV-negative and engages in high-risk behaviour, PrEP can be considered.

**Psoriasis: updates in biologic therapy, comorbidities and genetics**

Speakers: Jashin J. Wu, John Y.M. Koo, Wilson Liao

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The severity of psoriasis can be classified according to the body surface area (BSA) involvement. Mild psoriasis is less than 3% BSA, moderate is 4 to 10% and severe is greater than 10% of BSA. It is found that psoriasis gene is shared with other autoimmune diseases such as rheumatoid arthritis, vitiligo, type 1 diabetes and lupus. However, 37% of severe psoriasis patients do not have any treatment and 55% have topical treatment only. The Food and Drug Administration United States (FDA) placed a warning on biologics about serious infections that may cause death, frequent and even extrapulmonary tuberculosis and lymphoma. The
The speaker was worried that it might make the patients fearful of using biologics. Multiple studies suggested that biologics could actually decrease the death rate of psoriasis patients and there was no direct and strong evidence to support tuberculosis was related to biologics. Thus, the speaker suggested that biologics could be used safely if patients are monitored. Moreover, untreated psoriasis was associated with multiple co-morbidities. It has been shown that psoriasis increased the risk of chronic renal impairment and moderate to severe psoriasis was associated with chronic renal disease independent of traditional risk factors. It also increases the risk of asthma, COAD and periodontal diseases. Furthermore, it increases the risk of hypertension and vascular inflammation. However, the risk of myocardial infarction, aortic stiffness and carotid artherosclerosis are reduced after using TNF-α inhibitors. C-reactive protein, which may reflect the inflammation inside the body, is also reduced after using TNF-α inhibitors. Therefore, psoriasis-associated metabolic diseases can be reduced by biologics.

**Learning points:**
Psoriasis has some genetic predisposition and shares similar genes with other autoimmune diseases. Although FDA poses warnings on biologics, studies reveal that with adequate monitoring, biologics are safe.

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**Sex, Sores, Science and Surveillance: syphilis in the 21st century**

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Syphilis is caused by *Treponema pallidum* (TP) which is a spirochaete and cannot be cultured in the laboratory. It is transmitted through sexual contact, bloodborne route, congenitally and as an occupation hazard. TP can be infected through skin-to-skin or skin-to-mucosal contact. Therefore, condoms may not provide absolute protection. There is a 30 to 50% risk of getting infection after exposure. Primary syphilis classically presents as a chancre that is a painless indurated ulcer. It is very infectious at this stage. The reason why the chancre is painless is still not known, but a study in 1980 showed that the degenerative change of the terminal axon might explain the lack of pain in the chancre. Secondary syphilis commonly has systemic symptoms such as fever, malaise and lymphadenopathy. It typically presents as a papulosquamous rash on the trunk and limbs including the palms and soles. Mucosal patches and condyloma lata may also be present. In immunosuppressed patients, lues maligna which presents with a polymorphic, nodulo-ulcerative rash with systemic symptoms may be found. Afterwards, the disease enters the latent phase. There is an absence of mucocutaneous presentation and blood test is the only way to diagnose latent syphilis. There is up to 25% of false negative rate of VDRL or RPR in primary syphilis. It may be due to the prozone effect when the titre is very high. Therefore, one should dilute the sample to exclude the prozone effect and repeat the VDRL/RPR later to detect the serological changes. Neurosyphilis can occur in any stage of syphilis. According to US CDC guidelines, lumber puncture should be performed in patients with (1) neurological,
otological or ophthalmic signs and symptoms; (2) treatment failure and (3) evidence of active tertiary syphilis. Neurosyphilis is not related to HIV infection or CD4 count. Congenital syphilis is rare in United States, but is still a global problem, especially in Africa. It leads to spontaneous abortion, stillbirth, neonatal death and congenital syphilis in 10%, 10%, 20% and 20% of the cases respectively while 40% of the infected women would have healthy babies. Neonatal syphilis may present as sepsis, preterm delivery, low birth weight and hepatosplenomegaly and can be fatal. Early congenital syphilis occurs at three weeks to two years old. It may present with snuffles, rash and lymphadenopathy. It is often associated with growth delay, hepatitis, nephrotic syndrome and pseudoparalysis of the baby because of the bone pain. Late congenital syphilis is associated with clinical stigmata. It can damage the eighth cranial nerve causing sensorineural deafness and affect the eyes by causing interstitial keratitis and can also affect the bones causing frontal bossing, saddle nose and sabre shins as well as causing Hutchinson’s teeth and neurosyphilis. US CDC recommends that all pregnant women should be screened for syphilis in the first trimester of pregnancy, and that screening should be repeated in the third trimester in the high-risk population. Treatment of syphilis in pregnancy is benzathine penicillin as for other clinical groups. If there is penicillin allergy, desensitisation should be performed.

Learning points:
Syphilis is still common and clinical history, physical examination and blood screening help to detect syphilis early, especially in pregnant women. Lumber puncture should be performed if there are neurological symptoms and signs. Benzathine penicillin is the mainstay of treatment for syphilis.

Male genital dermatology: lessons learned from a male genital skin disease clinic
Speaker: Anthony Peter Hall
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Male genital skin problem is commonly non-infectious genital skin disease. As dermatologists, we must be familiar with the normal variants of the male genital skin conditions such as pearly penile papules, angiokeratoma and ectopic sebaceous gland (Fordyce spot). They may be misinterpreted as genital warts. Phimosis is difficulty in retraction of the foreskin. It can be physiological in childhood but pathological after puberty. Persistent phimosis after puberty is commonly due to lichen sclerosus and it should be treated by topical steroids before surgical circumcision is considered. Four common male genital dermatoses are irritant dermatitis, genital dysaethesia, lichen sclerosus and psoriasis. Five most important causes of papules or plaques in male genitalia are "PENIS": Psoriasis, Eczema, Neoplasm, Infections, Scabies. Psoriasis in the penis may not have scales especially for uncircumcised patients. It is better to look for evidence of psoriasis in other sites. Topical steroid is the treatment for penile psoriasis. The speaker suggested using potent steroid for a short period such as two to four weeks and then change to moderate or mild one. Vitamin D preparations are the second-line treatments which can be used as a monotherapy or combined with topical steroid. Calcineurin inhibitors may be the third-line treatment because it causes irritation in the genitalia. Biopsy should be considered to rule out malignant conditions such as Bowen's disease if the plaque is resistant to treatment. Irritant contact dermatitis is relatively common in genitalia. Removal of irritants such as soap substitution, skin moisturiser and topical steroid are the principal treatments.

Lichen sclerosus, lichen planus and Zoon’s balanitis are dermatoses with a predilection for male genitalia. Lichen sclerosus presents as
whitish patch with some contraction on the glans penis and foreskin, foreskin, i.e. acquired leading to difficulty in retracting the foreskin – acquired phimosis. A constriction of the distal penile shaft is formed after retraction of the tight foreskin and forming a waisting on the penile shaft. It can be treated by ultrapotent topical steroid such as clobetasol and circumcision. Studies suggested that there was a 4-8% risk of lichen sclerosis of male genitalia developing into penile squamous cell carcinoma (SCC) and 32 to 50% penile SCC had histological evidence of lichen sclerosus. Lichen planus presents as annular hyperkeratotic plaque. It may associate with some superficial erosions. Potent steroid is needed for penile lichen planus and systemic steroid is seldom required if the lesion is confined to the genitalia only.

Zoon's balanitis also presents as erythematous plaque with some erosions on the glans. It lasts for months to years. The aetiology is unknown but it may be caused by irritants or mild trauma. Topical steroid is the main treatment. Tarcolumus ointment 0.1% may be an alternative for topical steroid. Since Zoon's balanitis may be a reactive condition, circumcision may not be helpful.

Bowen's disease may present as a subtle erythematous macule or patch around the meatus with or without scales. Ninety percent of Bowen's disease is found in uncircumcised men. It is more commonly found on the glans and prepuce (erythroplasia of Queyrat) than at the shaft of penis (Bowen). There is a 5 to 33% risk of transformation into invasive squamous cell carcinoma. Treatment includes topical 5-fluorouracil (5-FU) or imiquimod, cryotherapy, surgical excision and photodynamic therapy. Bowenoid papulosis presents as multiple red or brown papules. It is associated with HPV 16 but the risk of SCC is unknown but is probably low. Topical imiquimod cream, 5-FU, cryotherapy, cauterisation and surgical removal are the possible treatments. Squamous cell carcinoma of the penis may be HPV related or HPV independent such as resulting from lichen sclerosus. Risk factors include poor hygiene, smoking, HPV related, chronic inflammatory dermatoses such as lichen sclerosus, phimosis and PUVA therapy.

**Learning points:**

One should be familiar with the normal variants of the genitalia to avoid misdiagnosis. Topical steroids, even ultrapotent steroid should be used in some dermatoses such as lichen sclerosus before tapering to moderate or mild strength topical steroid if the disease is controlled. Topical treatments such as imiquimod cream, 5-FU cream, cryotherapy and cauterisation could be used to treat pre-malignant conditions or squamous cell carcinoma in-situ.

**Herpes zoster: controversies and conundrums in treatment and prevention**


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Shingles in Latin means encircling the body and zoster in Greek means belt or girdle. There are one million cases in each year in the United States. There is a 10-30% life-time risk of developing herpes zoster. The varicella zoster virus belongs to the herpesvirus family. After the primary infection of chicken pox, the varicella zoster virus (VZV) will then enter the latent phase
in the dorsal root ganglion of the peripheral and cranial nerves. When the host immunity decreases, VZV reactivates along the dermatomal distribution. The reason why a particular dermatomal level is affected in reactivation is still unknown. It usually presents as multiple painful vesicular lesions along the dermatomes. It occurs on the trunk and in V1 region of the trigeminal nerve in more than 50% and 10-15% of the cases respectively. However, the presentation may be different in immunosuppressive patients or in children.

In immunosuppressed patients (e.g. due to HIV infection, immunosuppressive drugs, leukaemia or lymphoma patients), the risk of herpes zoster (HZ) is higher. There is a six-time higher risk in HIV-infected patients and HZ is more common in young age groups. Actually, HZ can occur at all CD4 levels, but with a low CD4 count, the risk of HZ is higher. Moreover, the duration and severity of HZ may be more significant in HIV patients. It can present as multiple dermatomal involvement and even disseminated HZ. Moreover, the HZ may be verrucous and the chance of resistance to acyclovir also increases in patients with a low CD4 count. HZ is also increased in the immune reconstitution inflammatory syndrome (IRIS). However, HIV patients have a lower risk of post-herpetic neuralgia after HZ. HZ is rare in paediatric patients. The differential diagnosis in children may include atypical hand-foot-month disease, herpes simplex infection, breakthrough of varicella after chicken pox vaccination. Immunodeficiency workup is not necessary in paediatric patients unless the HZ is severe, disseminated and recurrent. Tzanck smear is a traditional diagnostic method. The sensitive is 80% and specificity is 90%. It can be improved in experienced hands. Direct immunofluorescence assay is a quick and inexpensive diagnostic method. It can differentiate HSV I, HSV II and VZV. Nowadays, PCR provides a sensitive and specific way to diagnose HZ. However, it is expensive. Antiviral therapy is the mainstay of treatment. Aciclovir, valacyclovir and famciclovir are commonly used medications. They are guanosine analogues and inhibit the viral DNA by incorporating into DNA after phosphorylation by the viral thymidine kinase. VZV is less sensitive than HSV to these medications and the medications can help to shorten the duration of disease, decrease viral shedding and reduce the pain. However, it may not help to reduce the incidence of post-herpetic neuralgia. No topical treatment has been approved for the treatment of herpes zoster. There is an increase in aciclovir resistance in HIV patients with a low CD4 count. Vaccination is a good way to prevent herpes zoster. It is safe with not much systemic adverse effect. Local reaction like pain, erythema and swelling may happen at the injection site. It is a live attenuated vaccine and suggested by US CDC to vaccinate people who are older than 60 years old. Studies also provide evidence that the vaccine is helpful in people aged 50 to 59 years. However, zoster vaccine is contraindicated in pregnant women and those allergic to neomycin. It is not indicated for patients who are on immunosuppressants such as long term prednisolone >20 mg per day or biologics. In HIV patients, the vaccination should be delayed until the CD4 count is greater than 200/mm³. Patients with a history of rheumatoid arthritis, systemic lupus and inflammatory bowel disease may have a two to three times increased risk for HZ. It may be more severe and there is a higher chance of post-herpetic neuralgia. Preferably, these patients should be vaccinated before starting biologics or immunosuppressants if possible.

Learning points:
Herpes zoster is due to a decrease in the cell-mediated immunity to VZV. Atypical presentation may occur in immunosuppressed patients. Doctors can consider vaccinating these patients before starting immunosuppressants. Anti-viral therapy is the mainstay treatment for acute reactivation to reduce the pain, viral shedding and shortens the course of disease.