Dermatologic Manifestations in HIV Disease

(adopted from HIV Manual 3rd Edition, 2013)

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CME / CNE / PEM point accreditation (please refer to the attached test paper for the number of

credit points awarded)

Introduction

Skin disorders are commonly encountered in HIV-infected patients, and they may be the first manifestation of HIV disease. Up to 90% of HIV-infected persons suffer from skin problem during their course of illness. The frequency and distribution of dermatologic diseases in HIV infection vary widely. This can be partially explained by the difference in study design, stage of HIV disease, pattern of prevailing infections and use of HAART. In a cross-sectional study of 186 HIV positive patients in Hong Kong, 175 (94%) suffered from one or more cutaneous disorders. The most common skin disorder identified was fungal infection, followed by eczema and seborrhoeic dermatitis (*Box 17.1*).

In general, declining immunity is associated with increased number and severity of skin disorders.² Skin lesions are more likely to have unusual appearance and disease course, and could be recalcitrant to standard treatments in advanced HIV infection.

Box 17.1 Cutaneous disorders diagnosed in a cross sectional study in a HIV clinic in Hong Kong (n= 186)

utaneous disorders [#]	Number (%)	
Superficial fungal infections: tinea pedis, onychomycosis, tinea cruris, tinea corporis, pityriasis versicolor	89 (47.8)	
Eczema	49 (26.3)	
Seborrhoeic dermatitis	42 (22.6)	
Lipodystrophy	22 (11.8)	
Nail conditions: melanonychia, nail dystrophy, chronic paronychia, subungual haematoma, ingrown toenail	20 (10.8)	
Folliculitis: bacterial folliculitis, eosinophilic folliculitis, pityrosporum folliculitis	19 (10.2)	
Pruritic papular eruption	14 (7.5)	
Cheilitis / dry lips	11 (5.9)	
Viral infections: common warts, post-herpetic neuralgia, molluscum contagiosum	9 (4.8)	
Hyperpigmentation: melasma, easy suntan, generalised hyperpigmentation	9 (4.8)	
Drug reaction	6 (3.2)	

*Other conditions included exaggerated insect bite reaction, xerosis, keratosis pilaris, Kaposi's sarcoma, urticarial and vitiligo. An individual may have more than 1 dermatological condition, 175 (94%) had got one or more cutaneous disorder during their course of HIV infection, giving a total cumulative incidence of 528 dermatoses. One hundred and sixty (86%) were found to have one or more cutaneous disorders at the time of screening.

The advent of HAART has changed the spectrum of skin disorders by improving host immunity, which in turn reduces the occurrence of Kaposi's sarcoma (KS) and some of the skin conditions.³ However, the restoration of immunity especially in those with more advanced HIV disease have led to a change in the presentations of many opportunistic infections and diseases. These are referred as "immune reconstitution syndrome" (IRS) or "immune restoration disease" or "immune reconstitution inflammatory syndrome". The spectrum of dermatological manifestations in IRS is summarized in Box 17.2. HIV-infected patients are more likely than the general population to have adverse drug reactions. Antiretroviral agents, almost without exceptions, carries the risk of causing mucocutaneous adverse reactions (Box 17.3).^{5,6} Some of these adverse effects can be class specific whereas some are specific to the individual drug. The mechanism of these effects can be allergy, idiosyncratic, or pharmacological in nature. On the other hand, recognition of dermatological manifestations in HIV disease may be contributory to disease diagnosis, staging and choice of specific therapeutic agents. Skin diseases in people with HIV may cause significant morbidity and affect drug adherence. For example, a man who has sex with men may be prompted to have HIV testing with a KS blemish on the face and be driven to take HAART for the same rash. Likewise, a patient may be driven away from HAART because of lipodystrophy.

Box 17.2 Dermatological manifestation	ns of immune reconstitution syndrome
Opportunistic infections related	
Viral	
HSV Herpes simplex virus	Extensive or haemorrhagic lesions reported, may be associated with myelopathy or encephaltitis
VZV varicella zoster virus	High incidence of zoster in the initial months after initiation of HAART, usually uncomplicated and responsive to usual treatment
HHV 8 Human Herpes Virus	Inflammation and enlargement of existing lesion, lymphedema, occasionally new eruption, uncommon
Wart virus	Increase in incidence of oral warts, inflammation of existing warts
Molluscum poxvirus	Newly appearing molluscum, inflammation of existing lesions
Mycobacteria	
MAC Mycobacterium avium-intracellular e complex	Papulonodular lesions with pustules or subcutaneous abscess, often with systemic symptoms
MTB Mycobacterium tuberculosis	Nodular lesions, skin changes overlying inflamed lymph nodes
Leprosy	Reversal reaction
Fungi	
Cryptococcus	Unmasking occult infection, subcutaneous nodules
Candida	Inflamed angular cheilitis
Dermatophytes	Annular plaque with active margin
Non-infectious inflammatory skin disc	eases
Eosinophilic and other inflammatory folliculitis	New onset or flare of eosinophilic pustular folliculitis
Granulomatous reaction to tattoo	Precipitate foreign body reaction in existing tattoo

Lupus erythematosus	Onset of lupus erythematosus or tumidus after HAART reported		
Other reports include flare of acne, unmasking of histoplasmosis, accelerated course of leishmaniasis, precipitation of Reiter's syndrome, sarcoidosis, alopecia universalis and dermatofibromata.			

D 02	x 17.3 Adverse mu	acocutaneous effects of antirctroviral agents
		ranscriptase inhibitors (NRTI)
Cut	aneous adverse eff	ects are mostly specific to individual drug i.e. not class specific; mitochondrial rith this class may contribute to lipodystrophy which has a stronger relationship
•	Zidovudine	Mucocutaneous & nail hyperpigmentation, hypertrichosis, leucocytoclastic vasculitis, paronychia, fever associated with a variety of rash described as lichenoid, morbiliform, urticarial, erythema and edema, TEN
•	Stavudine	Peripheral oedema
•	Didanosine	Dry mouth, leucocytoclastic vasculitis, SJS, papuloerythroderma of Ofuji, alopecia
•	Abacavir	Rashes described as maculopapular, urticarial, EM, diffuse erythema, targetoid, Sweet's syndrome
•	Lamivudine	Allergic contact dermatitis
•	Emtricitabine	Dry skin, maculopapular, urticarial and vesicobullous rash; palmoplantar hyperpigmentation
Nu	cleotide reverse tr	anscriptase inhibitors (NTRTI)
	T	34 1996
	Tenofovir	Morbiliform to vesicular rash with mucosal involvement, urticarial; low incidence and usually self-limited
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Nev hyp • • Pro Cor	n- nucleoside reversitation has the highersensitivity syndrome. Nevirapine Efavirenz Etravirine otease inhibitors (Intribute to lipodystrome)	incidence and usually self-limited rse transcriptase inhibitors (NNRTI) thest incidence of morbiliform rash which may be part of systemic tome Morbiliform rash, DRESS SJS, AGEP, oral ulcer Morbiliform usually self-limited and hence HAART may not necessarily be ceased solely because of skin rash; history of nevirapine rash does not preclude the use of efavirenz Morbiliform, urticarial, erythema, pustular, dermatitis but usually resolved despite continuation of treatment; less commonly gynaecomastia, dry skin, hyperhidrosis, or lipodystrophy; <0.1% SJS, EM or as part of DRESS PI) rophy in varying degree and may have stronger relationship with central fat
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		therefore should be used with caution in people with history of sulfonamide reaction)
•	Atazanavir	Mild rash not requiring treatment cessation, asymptomatic jaundice
•	Tipranavir	Morbiliform, urticarial, photosensitive rash, mucocutaneous ulceration
•	Darunavir	"rash-related events" not otherwise specified, SJS, EM
Ent	try and Fusion inhi	ibitor
•	Enfuvirtide	injection site reactions common
•	Maraviroc	"rash" not otherwise specified

EM: erythema multiforme; SJS: Stevens Johnson syndrome; TEN: toxic epidermal necrolysis; DRESS: drug reaction with eosinophilia and systemic symptoms (abacavir hypersensitivity syndrome and systemic hypersensitivity syndrome associated with nevirapine fulfill most criteria of DRESS); AGEP: acute generalised exanthematous pustulosis

Approach to skin conditions in HIV/AIDS

Classification of HIV dermatoses

A myriad of skin disorders is implicated in managing people with HIV/AIDS. Some of the conditions are more specifically associated with HIV/AIDS.

Presentation of a skin disease in HIV disease may either be typical or atypical. Some examples are:

- (a) Typical clinical presentation of a common skin disease e.g. as seborrhoeic dermatitis
- (b) Atypical presentation of a common skin disease e.g. giant molluscum in an adult man
- (c) Typical presentation of an uncommon disease e.g. KS
- (d) Atypical presentation of an uncommon disease e.g. extrapulmonary pneumocystosis involving the external auditory canal
- (e) Unique condition in HIV disease e.g. lipodystrophy syndrome

The skin conditions associated with HIV/AIDS can be systematically classified by their pathogenesis, selected conditions of which are described in *Box 17.4*.

Box 17.4 Selected dermatological diseases in people with HIV/AIDS (a) Bacterial infection

Disease	Typical presentation	Atypical presentation	Diagnosis	Treatment	Remarks
Boils, folliculitis, impetigo and related conditions	Pustule as the primary skin lesion for boil and folliculitis; weeping macule or small patch with peripheral fine scale for impetigo; lesions commonly caused by <i>Staphylococcus</i> or <i>Streptococcus</i> , or <i>Pseudomonas</i> in other cases	Botryomycosis in form of subcutaneous nodules or plaques with ulcers or fistulae discharging purulent materials on scalp, axillae or groins; associated with Staphylococcus	Clinical; swab for culture	Antibiotics, antiseptics, with or without surgical drainage	Recurrent bacterial infection is a feature of HIV infection in children
Mycobacterium including TB	Varying appearances - nodules or plaque or localized cutaneous abscess, suppurative lymphadenitis, non-specific ulcerations as in direct infection; reactive tuberculids such as papulonecrotic papulonodules, panniculitis		Mainly by culture or histopathology supplemented by nucleic acid amplification tests.	Similar to that for systemic disease, according to the type of mycobacteria isolated and the immune status of the individual	
Bacillary angiomatosis	Vascular papules or nodules (pyogenic granuloma - like) as primary lesions, distributed over the face or upper trunk; important differential diagnosis for KS		By histopathology with special stain (e.g. Warthin Starry stain)	May include macrolide (or azalides) antibiotics, doxycycline; ciprofloxacin, rifampicin and septrin also have activity against the causative organism (<i>Bartonella sp.</i>)	Seldom encountered in Hong Kong

Box 17.4	Selected dermatological diseases in people with HIV/AIDS (Cont.)
(b) Funga	al infection

Disease	Typical presentation	Atypical presentation	Diagnosis	Treatment	Remarks
Superficial dermatophytosis	Annular lesion with active margin and central clearing in tinea corporis, faciale and cruris; diffuse hyperkeratosis or vesiculation in tinea pedis	Tinea faciale mimicking erythema multiforme or seborrhoeic dermatitis, and tinea pedis presenting as keratoderma blenorrhagica like lesion; Majocchi's granuloma; proximal white subungual onychomycocis (uncommon in normal host) well described in HIV	Microscopic examination and culture of scale/ nail/ hair sample obtained	Topical imidazoles or, Whitfield ointment; oral drugs - griseofulvin, itraconazole or terbinafine; fluconazole and posaconazole have also been used in nail infection	
Pityrosporum yeast	Pityriasis versicolor as classical lesion in form of hypopigmented macules with superficial fine powdery scale over upper trunk; pityrosporum folliculitis presenting with itchy monomorphic folliculitis or follicular papules over upper back, chest or face		Clinical or microscopic examination of scale obtained or histopathology	Topical or oral imidazoles (or triazole)	Related to seborrhoeic dermatitis
Candida sp	Oral thrush, angular cheilitis, intertrigo, balanitis, paronychia, balanitis and vaginal thrush as common manifestions	Median rhomboid glossitis	Clinical or microscopic examination, occasionally by culture	Topical or oral imidazoles (or triazoles)	Mucocutaneous candidiasis, usually by <i>C albican</i> , as one most common mucocutaneous condition in HIV disease
Penicilliosis	Typically as umbilicated papules simulating molluscum contagiosum	Ecthyma, folliculitis, subcutaneous nodule and morbilliform rash	Histopathology and/or culture of biopsy specimen	Amphotericin B or itraconazole	Skin involved in 75% of cases
Cryptococcus	Molluscum contagiosum like lesions	May mimic HSV, cellulitis, KS, or hypertrophic lesions like rhinophyma	Histopathology and/or appropriate culture	Amphotericin B or fluconazole ± flucytosine, itraconazole, voriconazole	

Box 17.4 Selected dermatological diseases in people with HIV/AIDS (Cont.) (c) Viral Infection

Disease	Typical presentation	Atypical presentation	Diagnosis	Treatment	Remarks
Acute, retroviral syndrome	Viral exanthema, occasional palm and sole involvement		HIV serological tests, may need to be repeated after window period	Antiretroviral treatment according to prevailing guidelines	
Varicella zoster	Primary skin lesions presenting as vesicles arranged in crops, distributed along one or more dermatomes; can be recurrent	Persistent non-healing ulcers, warty molluscum-like nodular lesion, disseminated and generalized involvement of the body	Mainly clinical; viral culture, direct immunofluorescence study or histopathology may sometimes be required for confirmation	Systemic acyclovir, valaciclovir, famciclovir	
Molluscum contagiosum	Primary skin lesion as white or red papules or small nodules with or without umbilication	Large lesions, may be warty and multiple with predilection for face in adult	Mainly clinical; histopathology may be required for confirmation in atypical cases	Curettage and iodinization commonly used; cryotherapy; spontaneous resolution after HAART reported	Off label use of imiquimod cream can be tried; cidofovir has been reportedly used

Box 17.4 Selected dermatological diseases in people with HIV/AIDS (Cont.) **(d) Inflammatory dermatoses**

Disease	Typical presentation	Atypical presentation	Diagnosis	Treatment	Remarks
Psoriasis	Typically an erythematous well demarcated plaque with silvery scale with predilection to the extensor surface of the limbs and body and scalp; may develop in patients with mild pre-existing psoriasis that suddenly undergoes severe exacerbation once AIDS develops, or may erupt spontaneously at some point after HIV seroconversion		Usually by clinical and occasionally by histopathology	Topical tar, salicylic acid, steroid, dithranol, calcipotriol, phototherapy (PUVA can theoretically suppress the body immunological function), and systemic agents such as retinoid, methotrexate (should be used with caution), use of biologics in people with HIV not adequately tested	
Seborrhoeic dermatitis	Poorly demarcated scaly erythematous patches involving glabella, nasolabial fold, external auditory canal, scalp, presternal area and occasionally the groins	Unusual sites such as the trunk and extremities may be affected; can be extensive and resistant to conventional treatment	Clinical examination	As pityrosporum yeast is thought to play an important role in this papulosquamous disorder, treatment is by combination of topical imidazole and mild topical steroid	Probably one of the commonest skin conditions encountered in patient with HIV infection, occurring in 85% of the patients at some points of their disease
Atopic dermatitis	Recurrence of pre-existing atopic dermatitis, which may have been in remission for some years; erythroderma has been reported; typically itchy skin rash in form of poorly demarcated erythematous papulovesicular lesions with weeping, scale crust in a characteristic distribution; different protean minor variations		Clinical examination (strict criteria as proposed by Hanafin or British Working Group should be referred)	Emollient, topical steroid, and occasionally phototherapy and short course of systemic steroid	
Xerosis, ichthyosis, and asteatotic dermatitis	Dry skin very common in patient with HIV infection; typically dry and flaky with or without excoriation marks		Mainly on clinical ground; important to rule out other important dermatological conditions with pruritus	Proper skin care and liberal use of emollient	Uncertain aetiology: probably the commonest cause of pruritus
Pruritic dermatoses in HIV	Pruritus as a common symptom in people with HIV. Heterogeneous: eosinophilic pustular folliculitis the more specific and better characterized entity, presenting with widespread excoriated follicular papules that involve head and neck, trunk and extremities, intact pustules unusually seen; important to exclude other conditions that may present with pruritus such as scabies, non-Hodgkin's lymphoma or dermatitis herpetiformis.		Clinical and histopathology	Oral isotretinoin, metronidazole, itraconazole, topical permethrin, calcineurin inhibitor or UVB reported with variable success in eosinophilic pustular folliculitis	Pruritic papular eruption originally described as a specific entity affecting people with HIV; now believed to be a feature of skin diseases of heterogeneous causes
Cutaneous drug reaction	Common manifestation of drug hypersensitivity; with septrin, anti-TB drugs, nevirapine and abacavir being the well reported causes; morbilliform rash probably the commonest type of drug rash; more serious reactions include SJS, TEN and DRESS.		Mainly by clinical assessment supplemented by histopathology and by exclusion	Withdrawal of implicating drug and supportive management; systemic steroid may be used in DRESS, Intravenous immunoglobulin may be used in TEN.	Abacavir hypersensitivity syndrome linked to HLA B*5701 (uncommon in Chinese), pretreatment screening should be considered

Box 17.4 Selected dermatological diseases in people with HIV/AIDS (Cont.) (e) Neoplastic diseases

Disease	Typical presentation	Atypical presentation	Diagnosis	Treatment	Remarks
Kaposi's sarcoma	Asymptomatic bluish/reddish macules as the common lesions; papulonodules or plague on nearly any sites on the body		Clinical diagnosis confirmed by histopathology	Can be expectant, local destructive, local chemotherapeutic or radiotherapy or systemic chemotherapy depending on the symptom and organ involvement; HAART may sometimes induce remission of KS	Chapter E29
Non-Hodgkin's lymphoma (NHL)	B-cell types of NHL occasionally presenting as fleshy skin papulonodules/ plaques; T-cell types as bizarre shaped patches, plaques or nodules with superficial scaling and inter/intra-lesional variations		Histopathology supplemented by immunohistochemical / molecular techniques	B-cell type NHL mainly treated by systemic chemotherapy; T-cell type NHL treated by chemophototherapy, radiotherapy (including total body electron beam), interferon, and systemic chemotherapy	
Cloacogenic carcinoma (or related dystrophic conditions)	Lesions can present as wart like papules (bowenoid papulosis/ vulval dystrophy) or squamous carcinoma like exophytic growth involving anogenital area		Histopathology	As for non-HIV infected person with similar conditions	Condition related to high risk HPV infection with pathogenesis similar as that for carcinoma of the cervix in female; disease incidence increased in HIV infected population

Diagnosis

The drug history, morphology of primary lesion (*Box 17.5*) and immune status CD4 (*Box 17.6*) are important clues to skin diagnoses.^{3,7,8} In many cases, HIV-associated skin diseases can be easily recognised on clinical grounds, especially in the early phase of HIV disease when clinical atypia is less frequent.

Lesional morphology	Differential diagnoses				
Morbiliform rash (measle like maculopapular erythematous)	 Acute retroviral syndrome Drug reaction Secondary syphilis 				
Erythroderma (rash involving more than 90% of skin surface)	 Drug reaction Psoriasis Norwegian scabies Seborrhoeic dermatitis 				
Folliculocentric inflammatory papules	 Folliculitis (bacterial, fungal, eosinophilic) Acne and acneiform eruptions Rosacea 				
Blistering	 Bullous impetigo Herpes (simplex or zoster) Drug reactions (EM, SJS, TEN) Porphyria cutanea tarda 				
Ulcer	 Herpes (simplex or zoster) CMV Mycobacterial infection Deep fungal infections Tumour (basal cell carcinoma and others) Factitious Aphthous ulcer 				

Box 17.6 Mucocutaneous diseases stratified by HIV disease stage			
Clinical stage	Rough CD4 count	Mucocutaneous conditions	
Early stage	>500 per μL	 Acute retroviral syndrome Kaposi's sarcoma Condyloma accuminata Vaginal thrush 	
Onset of immunosuppression	200-500 per μL	 Oral thrush Herpes simplex and zoster Recalcitrant seborrhoeic dermatitis Oral hairy leukoplakia Recalcitrant psoriasis Hyperkeratotic warts Nevirapine hypersensitivity 	
Significant immunosuppression	100-200 per μL	 Disseminated herpes Eosinophilic pustular folliculitis Wide spread and atypical Mollusca Extensive Kaposi's sarcoma 	
Advanced immunosuppression	<100 per μL	 Cutaneous penicilliosis Large non-healing herpes simplex Cutaneous cryptococosis Disseminated CMV 	

When diagnostic difficulty is encountered, skin biopsy should be considered for both histologic and microbiological evaluation. As HIV-infected persons frequently have more than one dermatosis, several biopsies may be necessary. Regardless, it would be simplistic to consider skin biopsy as the definitive method of diagnosis. The histopathological pattern may not be specific to a particular diagnosis. The unusual clinical presentation of a dermatosis may also extend to its histological pattern, for instance granuloma is not well formed in advanced HIV disease. Despite the use of special stain and culture, immunohistochemical or molecular technique, clinico-pathological correlation is often required to arrive at the more likely diagnosis.

Treatment

Although skin diseases are rarely life-threatening, many do severely hamper the quality of life of those affected. Therefore, good management starts with effective communication with those affected people. From another perspective, while the lifespan is prolonged by the use of HAART, many HIV-infected patients are troubled by drug-induced facial lipoatrophy which may affect the acceptability and adherence to HAART. Not only can there be cosmetic disfigurement, the intense pruritus due to eosinophilic folliculitis may severely impair the patients' quality-of-life. Therefore, management of these apparently minor conditions should not be overlooked.

A realistic therapeutic objective and expectation to outcomes should be explored and sensibly communicated between the two parties. Therapeutic objectives may include:

- (a) eradication or control of life threatening conditions,
- (b) prevention of complications or disease progression,
- (c) symptomatic relief,

- (d) restoration of functional status,
- (e) recovery of psychosocial well-being, and
- (f) improvement in cosmesis.

In most cases, treatment modality of skin diseases in HIV-positive patients is similar to that in HIV-negative ones. However, the immunosuppressive state and concurrent medication of the patient should always be considered in formulating treatment strategy. For instance, prolonged high-dose systemic steroid should be used with caution because of the immunosuppressive effects, while phototherapy must be treated with care as it has been shown to upregulate HIV transcription.⁹

References

- 1. Pennys NS. Skin manifestations of AIDS. London: Martin Dunitz, 1995.
- 2. Raju PV, Rao GR, Ramani TV, Vandana S. Skin disease: clinical indicator of immune status in human immunodeficiency virus (HIV) infection. *Int J Dermatol* 2005;44(8):646-9.
- 3. Rieger A, Chen TM, Cockerell CJ. Cutaneous Manifestations of HIV infection and HIV-related Disorders. In: Bolognia JL, Jorizzo JL, Rapini R. (eds). *Dermatology* 2nd ed. St. Louis (MO): Mosby Elsevier, 2008.
- 4. Lehloenya R, Meintjes G. Dermatologic manifestations of the immune reconstitution inflammatory syndrome. *Dermatol Clin* 2006;24(4):549-70.
- 5. Ward HA, Russo GG, Shrum J. Cutaneous manifestations of antiretroviral therapy. *J Am Acad Dermatol* 2002;46(2):284-93.
- 6. Introcaso CE, Hines JM, Kovarik CL. Cutaneous toxicities of antiretroviral therapy for HIV. *J Am Acad Dermatol* 2010;63(4):549-69. Part I Part II
- 7. Erdal E. Cutaneous manifestations of HIV. Medscape Reference drugs, diseases and procedures.
- 8. Jung AC, Paauw DS. Diagnosing HIV-related disease: using the CD4 count as a guide. *J Gen Intern Med* 1998;13(2):131-6.
- 9. Breuer-McHam J, Marshall G, Adu-Oppong A, Goller M, Mays S, Berger T, Lewis DE, Duvic M. Alterations in HIV expression in AIDS patients with psoriasis or pruritus treated with phototherapy. *J Am Acad Dermatol* 1999;40(1):48-60.

Test paper - Dermatologic Manifestations in HIV Disease (adopted from HIV Manual 3rd Edition, 2013)

Expiration Date: 21 April 2017

#
CME point / CNE point: 1 / PEM point: 0

- Please indicate one answer to each question.
- Answer these on the answer sheet and make submission by fax to Special Preventive Programme, Department of Health.

Please contact respective authorities directly for CME/CPD accreditation if it is not on listed below.

Accreditors	CME Point
Department of Health (for practising doctors who are not taking CME programme for specialists)	1
Anaesthesiologists	0
Community Medicine	1
Dental Surgeons	1
Emergency Medicine	1
Family Physicians	1
Obstetricians and Gynaecologists	0
Ophthalmologists	1
Orthopaedic Surgeons	1
Otorhinolaryngologists	pending
Paediatricians	pending
Pathologists	1
Physicians	0
Psychiatrists	1
Radiologists	1
Surgeons	1

- 1. Which of the following skin condition in HIV infected people is NOT caused by an infectious pathogen?
 - (a) Impetigo
 - (b) Molluscum contagiosum
 - (c) Bacillary angiomatosis
 - (d) Pityriasis versicolor
 - (e) None of the above
- 2. Which of the following skin condition is NOT commonly found in HIV infected people in Hong Kong?
 - a) Tinea corporis
 - b) Pityriasis versicolor
 - c) Histoplasmosis
 - d) Seborrhoeic dermatitis
 - e) Melanonychia
- 3. Which of the following skin condition is NOT a cause of ulcer in a person with HIV?
 - a) Cytomegalovirus infection (CMV)
 - b) Herpes zoster virus (VZV)
 - c) Herpes simplex virus infection (HSV)
 - d) Human herpesvirus 8 (HHV8)
 - e) Basal cell carcinoma

- 4. Which of the following matching of adverse effect of anti-retroviral drugs is NOT correct?
 - a) Sweet's syndrome and abacavir
 - b) Nail hyperpigmentation and zidovudine
 - c) Tetratogenicity and tenofovir
 - d) Drug Reaction with Eosinophilic and Systemic Syndrome (DRESS) and nevirapine
 - e) Paronychia and indinavir
- 5. Which of the following statement is NOT true?
 - a) Alopecia universalis may be the presentation of Immune Reconstitution Inflammatory Syndrome (IRIS).
 - b) New eruption of Kaposi's sarcoma (HHV8) after initiation of Anti-retroviral therapy (ART) means treatment failure and needs to stop the ART
 - c) Allergic contact dermatitis is a possible complication of Anti-retroviral therapy (ART)
 - d) Lipodystrophy may see in HIV infected people
 - e) Flare up acne may be seen after initiation of Anti-retroviral therapy (ART)
- 6. Which of the following is the skin manifestation of Immune Reconstitution Inflammatory Syndrome (IRIS)?
 - a) Increase in incidence of Herpes Zoster (HZV)
 - b) Inflammatory and enlargement of existing Kaposi's sarcoma (HHV8)
 - c) Increase in incidence of oral warts (HPV)
 - d) New onset or flare of eosinophilic folliculitis
 - e) Proximal white subungual onychomycosis
- 7. Concerning bacillary angiomatosis, which of the following is NOT correct?
 - a) Present like vascular papules or nodules
 - b) Usually distributed on face or upper trunk
 - c) The 2nd commonest skin manifestation in HIV infected patient in Hong Kong
 - d) Kaposi's sarcoma is its main differential diagnosis
 - e) Bartonella Sp. is the causative agents
- 8. Which of the following can occur in skin when the patient's CD4 count <100/uL?
 - a) Cutaneous cryptococcosis
 - b) Disseminated CMV infection
 - c) Cutaneous penicilliosis
 - d) Non-healing herpetic ulcer
 - e) All of the above
- 9. Which of the following condition is seldom present as blistering in HIV infected patient?
 - a) Herpes zoster infection
 - b) Impetigo
 - c) Severe Drug Reaction
 - d) Acute Retroviral syndrome
 - e) Porphyria cutanea tarda

- 10. In HIV infected patient, which of the following statement concerning seborrhoeic dermatitis is NOT true?
 - a) It may be resistant to the conventional treatment.
 - b) It may involve the trunk and extremities.
 - c) Oral terbinafine (Lamisil) is the first line treatment in HIV patient.
 - d) It is very common with probably over 80% occurrence in HIV infected patient.
 - e) Scalp, external auditory canal and occasionally groins can be involved