

**II. COMMON CLINICAL MANIFESTATIONS OF UNDIAGNOSED  
HIV INFECTION**

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## **II: COMMON CLINICAL MANIFESTATIONS OF UNDIAGNOSED HIV INFECTION**

### **INTRODUCTION**

This chapter briefly describes several dermatologic and oral complications of HIV infection that may be observed on routine examination in patients attending outpatient clinics. It is hoped that this chapter will assist clinicians in recognising and properly treating these conditions, many of which may present in individuals not yet diagnosed with HIV infection, prompting consideration of HIV testing. The appendix to this chapter includes a number of photographs of these conditions to better serve the clinician at the point of care.

For the sake of brevity, the list of conditions presented in this chapter is not intended to be comprehensive, nor is the management presented in great detail; only general principles of therapy for common presentations are offered. A more comprehensive review of many conditions presented herein can also be found in *Chapter V: Recommendations for the Treatment of Opportunistic Infections among Adults and Adolescents* and in *Chapter X: Diagnosis and Treatment of Opportunistic Infections among HIV-Exposed and -Infected Children*. The reader is also encouraged to consult an HIV expert clinician and/or other references for further information. *Chapter I* includes a list of some popular resources for clinical consultation.

### **COMMON DERMATOLOGIC MANIFESTATIONS OF HIV INFECTION**

Throughout the Caribbean, many patients infected with HIV initially present to a healthcare facility due to a skin complaint. Physicians practising in the region should therefore be knowledgeable about the skin conditions common in people living with HIV/AIDS (PLWHA). Many common skin disorders present in an aggressive form in PLWHA, especially in those with advanced HIV disease. Hence, any unusually aggressive skin condition should warrant consideration of undiagnosed HIV infection.

Long before the era of highly active antiretroviral therapy (HAART), physicians in the region had become familiar with many of the characteristic dermatologic presentations of HIV/AIDS. A clinical study conducted among HIV-infected patients attending a Bahamian dermatology clinic indicated that the leading HIV-associated skin disorders were seborrhoeic dermatitis, papular pruritic eruption, herpes zoster, hypo- and hyperpigmentation, xeroderma, folliculitis, and diffuse alopecia with loss of the natural peppercorn curl in Afro-Caribbean patients (e.g. the thinning and straightening of hair).

The introduction of HAART to the region reduced the incidence of skin diseases among patients receiving antiretroviral therapy. However, close monitoring of the skin is still recommended for all patients on HAART, as several of the antiretroviral (ARV) medications can cause severe drug eruptions including toxic epidermal necrolysis and Stevens-Johnson syndrome. It is also important to note that other skin eruptions may indicate treatment failure and clinical HIV disease progression. Referral to a dermatologist experienced in HIV skin management is recommended.

The management of these dermatological conditions remains a challenge due to a relative lack of proper diagnostic equipment and prescription skin medications in many islands through the region.

**Table 1: Common Dermatologic Manifestations of Undiagnosed HIV Infection**

<b>SKIN CONDITION</b>	<b>DIAGNOSTIC CLUES</b>	<b>USUAL TREATMENT</b>
<b>FUNGAL AND YEAST INFECTIONS</b>		
Candidiasis	Moist, scaling lesions with satellite papules. Intertriginous infections common. Fingernail infection often presents with paronychia.	Topical imidazoles useful, but systemic therapy may be needed, e.g. ketoconazole.
Cryptococcosis	Widespread, skin-coloured, dome-shaped, translucent papules or nodules. Often resembles molluscum contagiosum on face and neck.	Rule out <i>Cryptococcal</i> meningitis. Systemic amphotericin B or fluconazole 400-800mg q.d x 8 weeks then 200mg q.d.
Histoplasmosis	Slightly pink 2-6mm coetaneous papules to larger reddish plaques and multiple shallow crusted ulcerations.	Amphotericin B or itraconazole.
Seborrhoeic dermatitis	Erythematous dermatitis, scaly, itchy plaques with indistinct margins affecting scalp, face, ears, hairline, chest, upper back, axillae, and groin.	Mild topical steroid + imidazole usually effective. Oral imidazole occasionally needed. Regular use of dandruff shampoo containing selenium sulphide (Selsun <sup>®</sup> ), zinc pyrithione (Head & Shoulders <sup>®</sup> ), zincon, sulphur and salicylic acid (Sebulex <sup>®</sup> ), or polytar.
Dermatophytosis	Scaly annular plaques with active borders and central clearing, may become extensive with confluent hyperpigmented patches. Anogenital and nail involvement common.	Topical imidazole or terbinafine. For nail involvement, systemic fluconazole 150mg q.w x 4 weeks or terbinafine 250mg q.d x 2 weeks (6-12 weeks for toenails).
<b>VIRAL INFECTIONS</b>		
Herpes simplex	Grouped vesicular lesions; large erosions may be seen in advanced HIV disease.	Oral acyclovir or valacyclovir until lesions heal (approx. 1 week). IV therapy for CNS involvement. Chronic suppressive therapy often necessary.
Herpes zoster	Unilateral vesicular or bullous dermatomal eruption, sometimes multidermal; bullae may become haemorrhagic; persistent pain.	High-dose oral acyclovir (800mg 4-6x q.d), famciclovir 500mg po t.i.d, or valacyclovir (Valtrex <sup>®</sup> ) 1.0g t.i.d for 7-10 days. IV therapy in severe cases. Adjuvant topical antibiotics may be beneficial. Gabapentin, tri-cyclic antidepressants for post-herpetic neuralgia.

SKIN CONDITION	DIAGNOSTIC CLUES	USUAL TREATMENT
Molluscum contagiosum	2-5mm pearly, flesh-coloured papules typically on the face and anogenital region, often with central umbilication.	Chemical cauterisation (silver nitrate, podophyllin, 5-fluorouracil, phenol, tretinoin) or light cautery or cryotherapy of lesions. Often improves with HAART.
Human papillomavirus (warts, condyloma acuminata)	Diffuse flat and filiform lesions especially in anogenital region though can occur elsewhere.	Podophyllin chemical cautery, electrocautery, cryotherapy, surgery, or laser ablation.
<b>BACTERIAL INFECTIONS</b>		
<i>Staphylococcus aureus</i>	Cellulitis, abscesses, bullous impetigo, ecthyma, and folliculitis are all common.	Oral antibiotics with adjuvant topical therapy, drainage of abscesses; antipruritic therapy prn.
Secondary syphilis (due to <i>Treponema pallidum</i> infection)	Rash may take many forms. Copper-coloured lesions are often present on palms and soles. Serology may be negative in advanced HIV disease. CNS involvement common.	Benzathine penicillin (3 weekly IM doses of 2.4 million U).
Bacillary angiomatosis (due to <i>Bartonella henselae</i> infection)	Friable vascular papules, plaques, and subcutaneous nodules, usually tender. Lesions may be pedunculated, verrucous, and bleed extensively with trauma. Can be confused with Kaposi's sarcoma.	Erythromycin 500mg po q.6h or doxycycline 100mg b.i.d x 12 weeks.
<b>OTHER SKIN DISORDERS</b>		
Scabies	Excoriated, crusted, small papules, burrows, intense itching, worse at night.	Benzyl benzoate (12.5% in children and 25% in adults) or permethrin 5% cream x 1 day. Repeat in 7days. Antihistamines for relief of itching.
Crusted (Norwegian) scabies	Highly contagious disseminated scabies infection characterised by erythema, hyperkeratosis, and crusting. May be non-pruritic; bacterial superinfection can lead to sepsis.	Isolate patient if possible until therapy is complete. Permethrin 5% cream at least weekly until cutaneous manifestations clear. Ivermectin 6% ointment daily may be added; oral ivermectin also effective.
Eosinophilic folliculitis	Marked pruritus; discrete erythematous or hyperpigmented follicular papules on trunk, head, neck, and proximal extremities.	Astemizole 10mg q.d + topical steroid (oral imidazole use contraindicated with astemizole); UV phototherapy; permethrin; antihistamines for relief of itching.

SKIN CONDITION	DIAGNOSTIC CLUES	USUAL TREATMENT
Kaposi's sarcoma (KS)	Early lesions are round or irregular dark brown to violaceous or pinkish red macules, papules, or plaques. Usually non-tender. Often symmetrical along skin tension lines. Lesions can resemble ecchymoses. Oral lesions may precede skin lesions.	Numerous options depending on location and severity including local radiotherapy, cryotherapy, intralesional vinblastine, or interferon alpha; surgical excision. Often improves and may even remit with HAART. Look for visceral (e.g. GI, pulmonary) involvement.
Non-Hodgkin's lymphoma	Skin lesions are usually papules or nodules.	Chemotherapy.
Drug reactions and eruptions	TMP-SMX, erythromycin, dapsone, Dilantin®, NNRTIs (NVP>EFV) are common culprits. HIV+ patients have increased frequency of skin reactions to many drugs, ranging from a fixed drug eruption to generalised maculopapular eruption, exfoliative dermatitis, and even Stevens-Johnson syndrome, toxic epidermal necrolysis, or anaphylaxis.	Withdraw suspected drug. Stevens-Johnson syndrome and toxic epidermal necrolysis are managed as burns with intensive inpatient supportive care.
Psoriasis	Incidence and severity heightened in HIV disease. Secondary bacterial infection common.	Topical steroid or tar preparations, antimicrobial therapy for superinfection. Often improves with HAART.
Pruritic papular eruption	Scattered itchy papules and plaques predominantly on extremities. Recent research suggests arthropod (insect) bites followed by exaggerated immune response are responsible.	Topical steroids may help. Doxepin (starting at 10mg q.d and increased to as much as 150mg q.d) may be an effective antipruritic. Anecdotal evidence that condition improves with HAART.
Disturbance in pigmentation	Areas of hypo- or hyperpigmentation. Hyperpigmentation commonly seen in nails, skin, or oral mucosa of dark-skinned persons taking AZT.	Cosmetic cover creams. May improve with HAART. Consider substituting another NRTI for AZT.
Diffuse hair loss (alopaecia) or change in hair appearance	Hair becomes thin and sparse; loss of natural tight curl in Afro-Caribbean patients.	May improve with HAART.

SKIN CONDITION	DIAGNOSTIC CLUES	USUAL TREATMENT
Xeroderma	Severe dryness of the skin of face, trunk, and extremities.	Topical emollients prn (e.g. Aquaphor <sup>®</sup> ointment).
Prurigo nodularis	Hyperpigmented, hyperkeratotic excoriated itchy papules and nodules.	Oral antihistamines, potent topical steroids under occlusion.
Hyperpigmented or blue nails	Common, but benign, side effect of AZT.	Reassurance; consider substituting another NRTI for AZT if distressing to patient.

## **COMMON ORAL AND DENTAL MANIFESTATIONS OF HIV INFECTION**

Oral lesions are an important component of the spectrum of disease seen in HIV infection. There are almost forty different lesions reported in association with HIV disease. Presence of any of these lesions may be an early diagnostic indicator of immunodeficiency and HIV infection. Some oral lesions are also indicators of the disease's progression.

Current classification of many oral lesions of HIV disease is based on their strength of association with HIV infection:

### **Lesions Strongly Associated with HIV Infection:**

- Fungal Infections:
  - Pseudomembranous Candidosis
  - Erythematous Candidosis
  - Candidal Angular Cheilitis
- Hairy Leukoplakia
- Linear Gingival Erythema
- Necrotising Ulcerative Gingivitis
- Necrotising Ulcerative Periodontitis
- Necrotising Ulcerative Stomatitis
- Kaposi's Sarcoma
- Non-Hodgkin's Lymphoma

### **Lesions Less Commonly Associated with HIV Infection:**

- Viral Infections:
  - Herpes Simplex
  - Herpes Zoster
  - Condyloma Acuminata
  - Verruca Vulgaris
- Salivary Gland Disease:
  - Xerostomia
  - Salivary Gland Swelling
- Thrombocytopaenic Purpura
- Recurrent Aphthous Ulcers
- Melanotic Hyperpigmentation
- Cryptococcosis
- Histoplasmosis

**Table 2: Summary of Oral Manifestations of HIV/AIDS**

CONDITION/DISEASE	SALIENT CLINICAL FEATURES	DIAGNOSIS	TREATMENT	REMARKS
Pseudomembranous Candidosis	Soft white/yellow, curd-like plaques on oral mucosa. Deposits easily removable by gentle scraping.	Clinical grounds; smear stained by Gram's or PAS stain show candidal hyphae; candidal culture.	Topical antifungals:	
			<u>Mycostatin Pastilles:</u> Dissolve 1 tablet in mouth until gone, 4-5x q.d x 14 days.	Contains nystatin 200,000 units/tablet. Pastilles are more effective than oral suspension due to prolonged contact.
			<u>Mycostatin Oral Suspension:</u> Use 1 teaspoon 4-5x q.d, rinse and hold in mouth as long as possible before swallowing or spitting out (approximately 2 minutes).	Contains nystatin 100,000 units/ml. Do not eat or drink for 30 minutes following application.
			<u>Mycostatin Ointment or Cream:</u> Apply liberally to affected areas 4-5x q.d.	Contains nystatin 100,000 units/g. Denture-wearers should apply to denture surface prior to each insertion. For edentulous patients, mycostatin powder can be sprinkled on the denture.
			<u>Mycelex<sup>®</sup> Troche:</u> 10mg: dissolve 1 tablet in the mouth 5x q.d x 2 weeks.	Contains clotrimazole. Tablets contain sucrose; risk of dental caries with prolonged use (>3 months); care must be exercised in diabetic patients.
			<u>Nizoral<sup>®</sup>:</u> 200mg: take 1 tablet q.d x 10-14 days.	Contains ketoconazole. To be taken if <i>Candida</i> infection does not respond to Mycostatin. Potential for liver toxicity exists. LFT should be monitored with long term use (>3 months).

CONDITION/DISEASE	SALIENT CLINICAL FEATURES	DIAGNOSIS	TREATMENT	REMARKS
			<u>Nystatin:</u> (100,000 units) vaginal tablet dissolved in the mouth t.i.d x 2 weeks.	Contains nystatin.
			<u>Diflucan<sup>®</sup>:</u> 100mg: 2 tablets the first day and 1 tablet q.d x 10-14 days.	Contains fluconazole.
			<u>Mycolog Cream:</u> Apply to affected area after each meal and before bedtime.	Contains nystatin and triamcinolone. For candidal angular cheilitis. This often represents a mixed infection of <i>Candida</i> and other organisms.
			<u>Fungizone<sup>®</sup> Oral Suspension:</u> 1ml swish and swallow q.i.d between meals.	Contains amphotericin B. <b>NOTE:</b> When amphotericin B is used, pharmacologic antagonism may occur with ketoconazole and miconazole. It may increase toxicity of cyclosporin. Anti-neoplastic agents may increase the risk of toxicity of amphotericin-induced nephrotoxicity, bronchospasm, and hypotension. Patients receiving digitalis may present toxicity.
Erythematous Candidosis	Flat red patches on the dorsal surface of the tongue and hard palate.	As above.	As above.	As above.
Candidal Angular Cheilitis	Red, ulcerated, and fissured lesion at the angle of the mouth.	As above.	<u>Mycolog Cream:</u> (See above.)	Occasionally this may be caused by a mixed infection.

CONDITION/DISEASE	SALIENT CLINICAL FEATURES	DIAGNOSIS	TREATMENT	REMARKS
Hairy Leukoplakia (Oral Hairy Leukoplakia)	Asymptomatic bilateral, vertically corrugated or hairy white lesions on the lateral borders of the tongue.	Clinical and histological; demonstration of the virus; (EBV) by in situ hybridisation techniques or PCR	<u>Zovirax® (Acyclovir):</u> 200mg: 1 capsule q.6h x 2 weeks. Surgery, cryotherapy, or application of podophyllin.	Systemic administration causes some regression of HL. HL is not a premalignant lesion.
Linear Gingival Erythema	Well-demarcated, linear band of intense redness along the gingival margins.	Clinical	No treatment is necessary.	Does not respond to oral prophylaxis.
Necrotising Ulcerative Gingivitis	Painful ulceration of the interdental papillae associated with halitosis and spontaneous gingival bleeding.	Clinical; smear for identification of fusospirochetal organisms.	<u>Metronidazole:</u> 500mg: t.i.d x 7 days. Oral prophylaxis (scaling and debridement) is needed for these patients.	Use with caution in patients with blood dyscrasias, liver impairment, CNS/renal disease. Metronidazole increases the bleeding tendency in those on warfarin. No alcohol to be consumed during the treatment with metronidazole. May recur. Referral to dentist for management.
Necrotising Ulcerative Periodontitis (NUP)	Rapidly progressive periodontal disease resulting in bone loss.	Clinical; radiological	As above. Debridement of necrotic tissue.	Common cause of tooth loss; referral to dentist for management.
Necrotising Ulcerative Stomatitis	Extension of NUP into soft tissues. Bone sequestra.	Clinical; radiological	As above. Debridement of necrotic tissue.	Referral to dentist for management.
Kaposi's Sarcoma	Painless purple/violaceous lesions on palatal/anterior gingival mucosa; later becomes raised and ulcerated.	Clinical; histological	Surgery Cryotherapy Radiotherapy and intralesional injection of vincristine	Referral to an oncologist or specialist for management.

CONDITION/DISEASE	SALIENT CLINICAL FEATURES	DIAGNOSIS	TREATMENT	REMARKS
Non-Hodgkin's Sarcoma	Rapidly enlarging rubbery mass in the tonsillar fossa, palate, or gingival.	Clinical; histological	Surgery Radiotherapy Chemotherapy	Referral to an oncologist.
Herpes Simplex (HSV)	Clusters of painful, small vesicles/ulcers on palate or gingivae. Most cases of HSV infections are recurrent. Herpes labialis lesions are on the vermilion or mucocutaneous junction on the lips; form crusts on rupture. Herpes labialis is also known as cold sores.	Clinical; smear for viral inclusion bodies	<u>Zovirax® (Acyclovir):</u> 200mg: 1 capsule q.6h x 2 weeks. <u>Denavir® (Penciclovir) 1% Cream:</u> Apply locally q.2h x 4 days. <u>Vira-A 1% (Vidarabine) Ointment:</u> Apply to affected areas q.i.d.	Use with caution in patients with renal, neurologic, and hepatic diseases.  Contraindications: hypersensitivity to the drug.
Herpes Zoster	Prodrome of pain, multiple vesicles on facial skin, lips, and intraoral structures. Follows the nerve distribution. May be complicated by post-herpetic neuralgia.	Clinical	As above. <u>Carbamazepine (for post-herpetic neuralgia):</u> 200mg: b.i.d to start; 800-1,200mg q.d (in divided doses) x 2 weeks.	
Condyloma Acuminata (Verruca Vulgaris)	Warts are nodular or cauliflower-like in appearance, often multiple.	Clinical; histological	Surgery CO2 laser surgery	Caused by human papillomavirus; uncommon in oral tissues.

CONDITION/DISEASE	SALIENT CLINICAL FEATURES	DIAGNOSIS	TREATMENT	REMARKS
Xerostomia	Dry mouth, often with fissured tongue. Promotes dental caries.	Clinical	Artificial saliva <u>Sodium Carboxymethylcellulose (Baker-Perkins) 0.5% Aqueous Solution:</u> To be used as a rinse as needed. Any of the following: Xerolube <sup>®</sup> /Moi-Stir <sup>®</sup> /MouthKote <sup>®</sup> / Optimoist <sup>™</sup> /Salivart <sup>®</sup>	Sucking ice cubes or lemon drops can be helpful.
Salivary Gland Swelling	Unilateral/bilateral salivary gland swellings.	Clinical	If xerostomia is present, as above.	If xerostomia is present, as above.
Thrombocytopenic Purpura	Bleeding tendencies; petechiae on oral mucosa.	Clinical; platelet count	Platelet transfusions in severe platelet deficiency.	No dental surgical intervention unless platelet numbers are restored.
Melanotic Hyperpigmentation	Melanotic linear lesions on the gingivae.	Clinical	No treatment is necessary.	Due to ARV drug reaction.
Cryptococcosis	Necrotic ulcerative lesions.	Clinical; smear culture	Antifungal treatment.	Oral involvement is rare.
Histoplasmosis	Necrotic growth/ulcers.	As above.	As above.	As above.
Erythema Multiforme	Ulcerative lip and intraoral lesions.	Clinical	Withdrawal of the drug. Sometimes antiviral drugs help.	Referral to a specialist.
Lichenoid Reactions	White lace-like lesions on the oral mucosa.	Clinical; histological	Topical steroid application. Kenalog <sup>®</sup> (triamcinolone acetonide) in Orabase cream 3-4x q.d x 1 week.	Withdrawal of cause if known.
Tuberculous Ulcers	Ulcerative lesions usually on the tongue or gingivae. Usually patient has pulmonary TB.	Clinical; histological (AFB stain); chest x-ray; tests for TB	Treat the systemic disease with anti-TB drugs.	Though TB is on the increase, oral involvement is uncommon.

<b>CONDITION/DISEASE</b>	<b>SALIENT CLINICAL FEATURES</b>	<b>DIAGNOSIS</b>	<b>TREATMENT</b>	<b>REMARKS</b>
Trigeminal Neuralgia	Shock-like pain along the distribution of the trigeminal nerve.	History	Carbamazepine	Uncommon
Facial Palsy	Unilateral paresthaesia of the face.	History; clinical	Sometimes antiviral medications help.	Uncommon
Dental Caries	Dental decay.	Clinical	Early detection and appropriate treatment.	Increased dental caries experience in HIV patients due to poor oral hygiene, xerostomia, etc.