

HIV-related skin conditions

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Dermatological conditions are common in all stages of human immunodeficiency virus (HIV) infection. As the skin is regularly observed by patients and easily examined by health care workers, dermatological conditions represent a good opportunity for early diagnosis of HIV.

Introduction

In the Asian and Pacific regions, the initial patient presentation with HIV is often late and often manifests by mucocutaneous complications consistent with falling cell counts and immunity. The range of common skin presentations of HIV is listed in Table 9.1. Studies have demonstrated the inverse relationship between skin disease and cell counts in HIV.¹ Skin manifestations of HIV can present as infectious, non-infectious and neoplastic disease.

Table 9.1: Common dermatological presentations of HIV

HIV likely

Inflammatory

Seroconversion-like eruption

Infective

Cutaneous *Cryptococcus*

Cutaneous cytomegalovirus

Oral candidiasis

Cutaneous tuberculosis or other mycobacterial lesions e.g. *Mycobacterium avium intracellulare* complex

Disseminated fungal infections

Bacillary angiomatosis (*Bartonella henselae* infection)

Other

Kaposi's sarcoma (associated HHV8 infection)

Eosinophilic folliculitis

Oral hairy leukoplakia (associated with Epstein-Barr virus infection)

Anal carcinoma

Lipoatrophy

Be suspicious of HIV

Inflammatory

Severe pruritus (pruritic papular eruption may be due to a florid reaction to insect bites)

Severe drug eruption

Infective

Human papillomavirus (warts, *Condyloma acuminata*)

Extensive molluscum contagiosum

Herpes zoster

Herpes simplex virus

Crusted scabies (Norwegian scabies)

Primary syphilis (co-infection with HIV)

*Penicillium marneffe*i cutaneous lesions

Recognising the HIV-related skin conditions may enable initial HIV diagnosis and also provide clinical confidence in the predicted degree of immunosuppression where CD4 counts are not readily available. Whereas some cutaneous conditions such as oral candidiasis, extensive molluscum contagiosum, eosinophilic pustular folliculitis, cryptococcosis or Kaposi's sarcoma are highly suggestive of HIV disease by their mere presence, other conditions common in the general population are distinguished in HIV infection by their atypical presentation, severity, frequency of recurrence or recalcitrant nature.²

Clinical presentations

Presentation of skin disease in HIV may either be typical or atypical:

- i) Typical presentation of a common skin disease e.g. seborrhoeic dermatitis
- ii) Atypical presentation of common disease e.g. extensive warts
- iii) Typical presentation of an uncommon disease e.g. Kaposi's sarcoma
- iv) Atypical presentation of uncommon disease e.g. cutaneous tuberculosis
- v) Unique condition in HIV e.g. oral hairy leukoplakia, lipoatrophy.

Seroconversion illness

The seroconversion eruption classically presents as a transient, generalised measles-like eruption on the trunk and extremities of the body but may be associated with vesicles and oral ulcers (Figure 9.1). Systemic features include fever, lethargy, myalgias and lymphadenopathy. This condition may go unnoticed by the patient.



Figure 9.1: Seroconversion eruptions. Used with permission from Professor J Gold, Albion Street Clinic, Sydney.

Timeline of cutaneous change with the loss of CD4 cells

HIV-related skin change represents a continuum along which patients may present (Figure 9.2). After seroconversion, skin diseases may follow along general population demographics with no signs of infection during early asymptomatic HIV disease.

In the next stage of HIV, skin presentations represent disease progression with opportunistic infections or acquired immunodeficiency syndrome (AIDS)-defining illnesses due to falling immunity. Since the advent of antiretroviral therapy, HIV skin disease is also seen in the clinical context of immune reconstitution inflammatory syndrome, with a spectrum of systemic or local inflammatory, infective, autoimmune or malignant disease with rising cell counts.^{3,4}

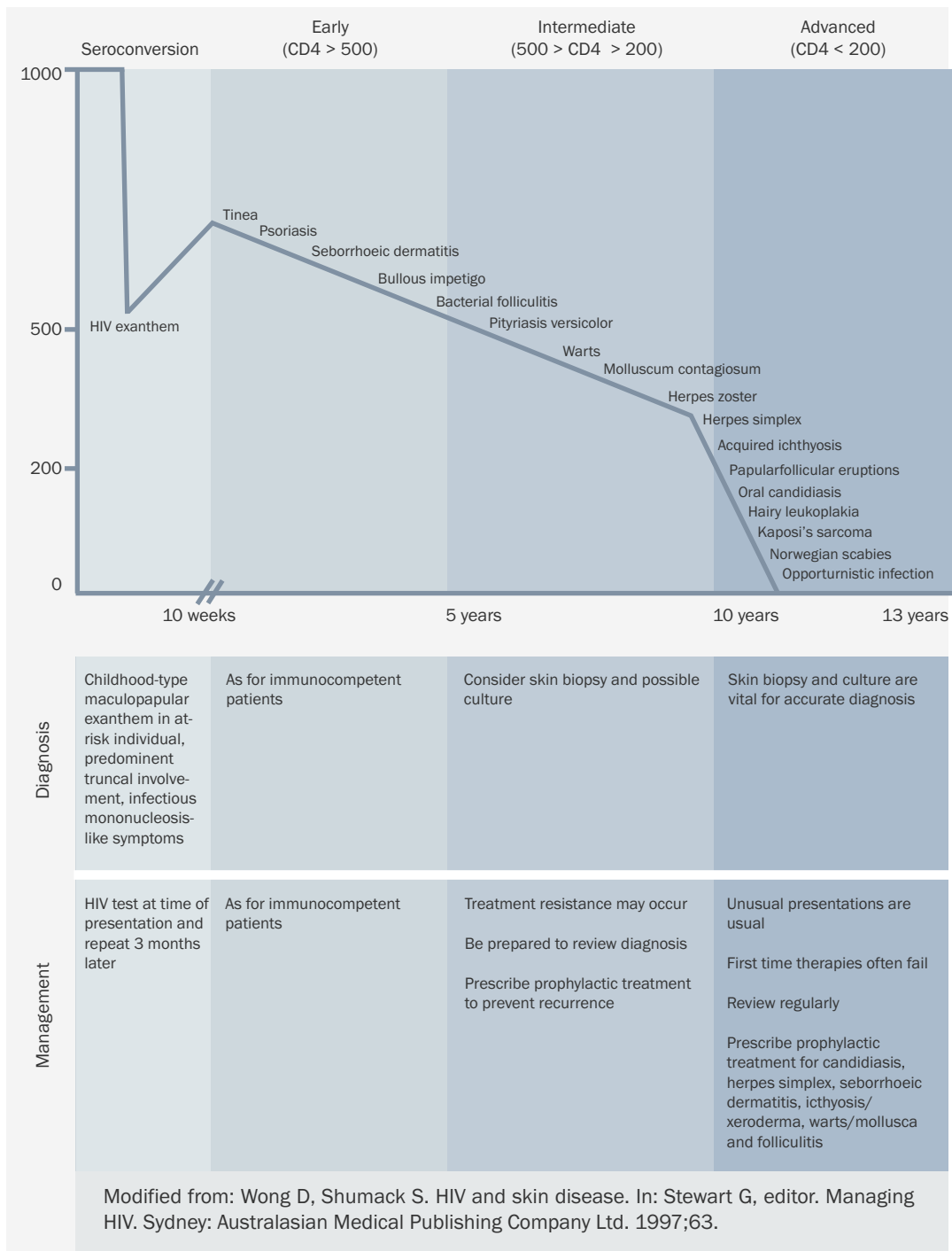


Figure 9.2: Timeline of cutaneous change with the loss of CD4 cells

Viral infections

Herpes (varicella) zoster

HIV should be considered in patients less than 40 years old presenting with herpes zoster. The typical presentation is a grouped vesicular (blistering) eruption involving one or more dermatomes with prodromal pain.^{5,6} The lesions become pustular and haemorrhagic within a few days, then crusting and scarring occurs (Figure 9.3). In HIV, the ulceration is often more extensive, deeper, prolonged, and the scarring more severe. Atypical, disseminated and chronic herpes zoster infections are usually in the setting of advanced HIV disease or immune reconstitution inflammatory syndrome.⁷ In children with HIV who develop chickenpox, there is a higher risk of subsequently developing herpes zoster and they are more likely to have recurrent episodes.⁸



Figure 9.3: Hand involvement of herpes zoster. Used with permission from the American Academy of Dermatology.

Herpes simplex viruses

These viruses include herpes simplex virus 1 and 2 (HSV-1 and HSV-2). They are common causes of acute and chronic skin lesions of grouped vesicles on an erythematous base (Figure 9.4). Chronic herpes simplex virus is more common in HIV and may present as indolent perioral and anogenital ulcerations, which may be painful (Table 9.2).

Recently studies have shown the association between HSV-2 infection and the risk of acquiring HIV. HIV-1 is shed from genital ulcers caused by HSV-2.⁹



Figure 9.4: Perianal herpes simplex. Used with permission from the American Academy of Dermatology.

Human papillomavirus

Human papillomavirus commonly causes warts in the context of both the general population and those with HIV infection. Warts in the context of HIV may be more pronounced, recalcitrant to therapy and in more unusual locations such as:

The forearm (Figure 9.5):

Condition	Affected area of the body
Herpes labialis	Lips and perioral area
Herpes genitalis	Genital area
Herpes gladiatorum	Buttocks
Herpetic whitlow	Fingers and around the nails
Herpetic keratoconjunctivitis	Eyes
Eczema herpeticum	Areas of eczema (may be widespread)
Neonatal herpes	In newborns
Herpes encephalitis	Central nervous system



Figure 9.5: Inflamed, extensive flat warts of the forearm, more obvious as they resolve after ART commenced. Used with permission from Dr M Whitfeld of St Vincent's Hospital, Sydney.

Lips (Figure 9.6):



Figure 9.6: Unusual location lip wart in HIV. Used with permission from Dr M Whitfeld of St Vincent's Hospital, Sydney.

Fungal infection

Fungal infections may present as persistent and recurrent skin disorders. Common superficial fungal infections include candidiasis and generalised dermatophytosis caused by *Trichophyton rubrum*. Deep fungal infections of note include cryptococcosis, histoplasmosis or penicilliosis which may signify systemic disease.

Penicillium marneffe is endemic in tropical Asia and can cause a fatal systemic mycosis in patients with HIV. It is the third most common opportunistic infection in patients with AIDS in Asia after tuberculosis and *Cryptococcus*. Disseminated *P. marneffe* infection in HIV can present as cutaneous lesions, appearing in 75% of patients who have penicilliosis.

Typical skin lesions are umbilicated papules with a central necrotic core on the face and neck, less commonly on the limbs and torso. The differential diagnosis includes molluscum contagiosum, histoplasma and *Cryptococcus*.¹⁰

Cutaneous cryptococcosis may manifest with cellulitis, papules, plaques, ulcers or translucent papules with central umbilication, resembling molluscum contagiosum. Cutaneous histoplasmosis is due to haematogenous spread and is endemic in South-East Asia. It can also present with papules, ulcers, acneiform or cellulitis-like eruptions.^{7, 11}

Seborrhoeic dermatitis is a common condition, affecting as much as 85% of patients with HIV.¹² It can present at any CD4 cell count, but with deteriorating counts it is often extensive, more severe and has a reduced response to treatment. Pityrosporum yeast (*Malassezia*) has a role in this disease. Patients with HIV characteristically have more erythema and extensive involvement in the sebaceous areas of the scalp and nasolabial folds than those without HIV (Figure 9.7). Sites such as the chest, back, axillae and intertriginous zones are more commonly involved.¹³

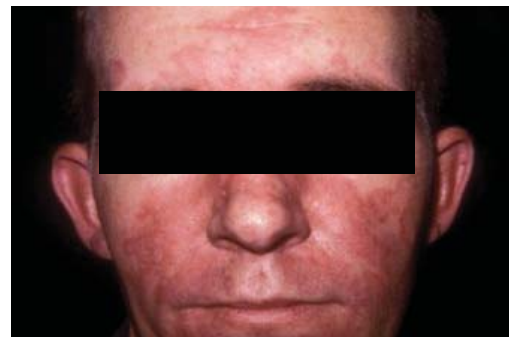


Figure 9.7: Photo of marked facial seborrhoeic dermatitis in the setting of HIV. Used with permission from Dr Toby Maurer, University of California San Francisco.

Other Infections

Syphilis

With the resurgence of clinical presentations of syphilis, syphilitic chancres should alert the clinician to the possibility of HIV; they are believed to increase HIV transmission.

Chancres are often more severe in the setting of HIV.^{14,15} The primary chancre presents as a painless ulcer 14-21 days after exposure (but often up to 90 days), and may be on the genitalia, perianal area, anal canal or oral cavity. Secondary syphilis has a wide variety of presentations, however, it is most commonly widespread and maculopapular or papulos-quamous in morphology.¹⁶

The differential diagnosis of secondary syphilis is often broad and multiple causes are possible in the general population and in the setting of HIV, including pityriasis rosea, drug eruptions, psoriasis, lichen planus and acute febrile exanthems.¹⁷ Concurrent primary and secondary syphilis are more common in HIV.

Scabies

In the setting of patients with HIV infection, the classic form as well as crusted scabies can occur. The classic form can occur at any CD4 cell count, while crusted scabies occurs at CD4 counts below 150 cells/ μ L. Classic scabies presents as papulovesicular lesions (Figure 9.8). The distribution varies, favouring the wrists, interdigital web spaces, elbows, axillae, breasts and genitals. Due to the associated pruritus and excoriation, bacterial superinfection may occur with impetigo, cellulitis and in some cases fatal sepsis.¹⁸ With HIV, the number of mites can increase unchecked, thus producing a more severe form of scabies or crusted scabies, in which there is marked thickening, often plaques, papules and crusting of the skin, particularly on the hands. The entire body including the head may be involved.^{19,25}



Figure 9.8: Exaggerated scabies of the hand. Used with permission from HIV Treatment and Care, Family Health International, Vietnam.

For **Molluscum contagiosum** see Chapter 7, HIV-related eye conditions.

Malignancy

Kaposi's sarcoma presents often with pigmentation evolving from erythematous macules of the skin that can develop into plaques and nodules, may ulcerate or disseminate and commonly involves the mucosa (Figure 9.9). It presents most frequently with CD4 counts below 200 cells/ μ L but can occur at any stage.^{20,15}

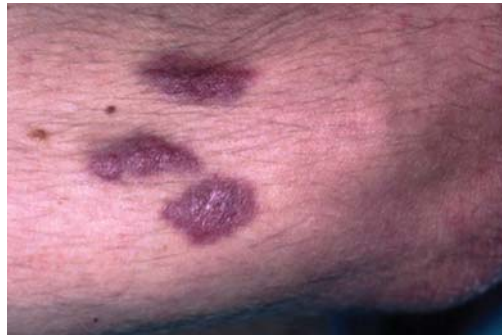


Figure 9.9: Kaposi's sarcoma of the forearm. Used with permission from Dr M Whitfeld of St Vincent's Hospital, Sydney.

Anal carcinoma, penile intraepithelial neoplasia and **cervical intraepithelial neoplasia** are papillomavirus-associated malignancies that can be more common, progressive and aggressive in those with HIV. Perianal, anal and penile intraepithelial neoplasia classically present as velvety erythematous or hyperpigmented defined plaques.^{16,17}

Other presentations

For **oral candidiasis** and **oral hairy leukoplakia** see Chapter 6, HIV-related oral and gastrointestinal conditions.

Eosinophilic folliculitis

Eosinophilic folliculitis presents as intensely pruritic 2-3 mm pruritic, erythematous, oedematous, urticarial papules centred around follicles and may have central vesicles or pustules.

The distribution is over the forehead, neck, shoulders, trunk and upper arms.

Secondary changes resulting from scratching are common, and include excoriations with secondary staphylococcal infection, prurigo nodularis, lichen simplex chronicus and post-inflammatory pigmentary changes. Clinically, it is most commonly seen in those not on antiretroviral therapy with advanced HIV with CD4 cell counts below 300 cells/ μ L.^{3,18}

Pruritus

Itch is one of the most common symptoms in patients with HIV and has multiple causes including skin infections, infestations, insect bites, papulosquamous disorders, xerosis and drug reactions (Figure 9.10).



Figure 9.10: Left arm demonstrating the presentation of papular pruritic eruption (PPE) of HIV. Used with permission from Dr Toby Maurer of University of California, San Francisco.

Adverse drug reactions on and off antiretroviral therapy

Drug eruptions are common and can present in a variety of contexts both on and off antiretroviral therapy. Drug eruptions are the most common cause of erythroderma in patients with HIV. Commonly measles-like drug eruptions can occur in as many as 65% of patients on sulfamethoxazole for *Pneumocystis pneumonia* treatment and prophylaxis.

Erythematous macules and papules can become generalised, persisting even after therapy cessation. Sulfonamides also cause urticaria, erythema multiforme, Steven Johnson's syndrome, and potentially life-threatening skin shedding called toxic epidermal necrolysis. Other frequently used medications that can cause toxic epidermal necrolysis in undiagnosed HIV include penicillin antibiotics or fluconazole. Antiretroviral drugs such as nevirapine can cause mild to severe skin rashes, including toxic epidermal necrolysis, but rashes associated with other antiretroviral drugs are usually not severe.^{19,20}

Case study 9.1

Mr AS is a 39-year-old man. He is a homosexual and has a history of injecting drug use. Recently he has been given a course of penicillin antibiotic therapy for a newly diagnosed penile syphilitic chancre. He has developed diffuse, total body erythema with an additional rash on his hands and back following his first dose of antibiotics (Figures 9.11 and 9.12).



Figure 9.11: Skin rash on the hands. Used with permission from HIV Treatment and Care, Family Health International, Vietnam.

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Case study 9.1 (Continued)



Figure 9.12: Skin rash on the back. Used with permission from HIV Treatment and Care, Family Health International, Vietnam.

Questions to consider

- Could it be HIV – when and how would you do an HIV test?
- What is your differential diagnosis of this skin rash?
- What other clinical conditions do you need to think about?
- What investigations are necessary?

He tested positive for HIV (rapid and confirmatory ELISA tests) and a rapid plasma reagin (RPR) test & a Venereal Disease Research Laboratory test were positive for *Treponema pallidum*. This skin eruption was thought to be due to a drug reaction to the penicillin or syphilis.

Therapy options

- Benzathine penicillin G 1.8 g (2.4 million units) intramuscularly as one dose followed by procaine penicillin 3 g (3 million units) intramuscularly daily plus probenecid 500 mg orally every 6 hour a day for 10 days.
- For patients who are allergic to penicillin: doxycycline 200 mg orally daily for 20 days or tetracycline HCl 500 mg orally 6 hourly for 20 days.

Conclusion

Given the visual nature of skin disease, being familiar with cutaneous signs of HIV and being able to determine immune status by the examination of the skin are of great value, particularly in resource-limited settings. It is important to suspect HIV in patients presenting with recalcitrant, recurrent or multiple skin conditions. These may complicate internal whole body disease i.e. systemic illness. Early recognition of HIV presenting as skin disease is essential for initiation of management of both the dermatological disease and HIV.

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