CUTANEOUS MANIFESTATIONS OF HIV/AIDS: PART 2

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VIRAL INFECTIONS

The insidious damage to the immune system by the human immunodeficiency virus results in increasing susceptibility to opportunistic viral infections. These can be localised, widespread, confined to the skin, or systemic. They can cause mild though disfiguring lesions such as molluscum contagiosum (MCV), or lead to life-threatening infections such as human papillomavirus (HPV-induced squamous cell carcinoma.

Viral opportunistic infections represent activation of subclinical infection (e.g. HPV, MCV) or reactivation of latent infection, e.g. herpes simplex virus (HSV 1 and 2) or varicella zoster virus (VZV). The incidence of opportunistic viral infections has diminished remarkably with the advent of highly active antiretroviral therapy (HAART).

HERPES SIMPLEX VIRUS 1 AND 2 INFECTIONS

Chronic herpetic infection was recognised early as a sign of chronic immunosuppression and as a marker for the presence of HIV infection, particularly in young adults. There is a sharp rise in the incidence of HSV infection with CD4 counts below 50. Herpes simplex infection is so common in our patients that we can almost assume that most wet-crusted lesions are herpetic until proven otherwise. A typical presentations are the rule. With more advanced HIV disease, lesions tend to be subacute or chronic and indolent and response to oral antiviral therapy tends to be less prompt. The presence of mucocutaneous herpes simplex infection for more than 1 month is classified as an AIDS- defining illness. In 65% of patients with recurrent erythema multiforme there is a history of herpes labialis or genitalis. This usually precedes the erythema multiforme by several days to weeks and occasionally may coincide with the herpes lesions.

With increasing immunocompromise, recurrent HSV infection may become persistent and progressive. The lesions are typically painful and occur at the typical sites – perioral, anogenital and digital (Fig. 1). They enlarge and deepen into painful ulcers (Fig. 2). When diagnosis is in doubt, a tzanck smear or viral culture of blister fluid of an early lesion (< 72 hours) is recommended; this usually takes about 1 - 5 days. Viral culture is the easiest way to make a diagnosis and can differentiate HSV 1 from HSV 2, but lesions must be in an early stage. If lesions are atypical or have been present for some time, other diagnostic modalities such as biopsy or polymerase chain reaction (PCR) may be considered.

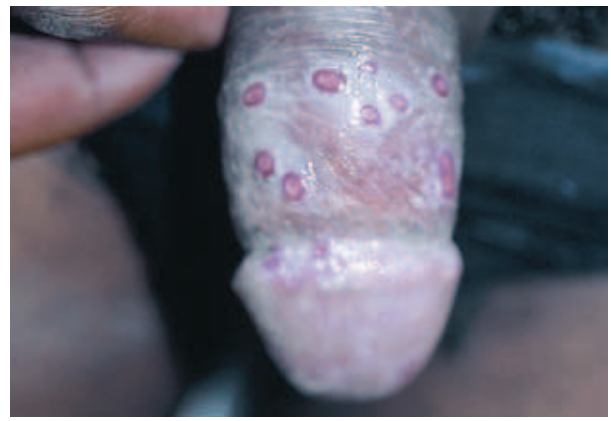

Fig. 1. Herpes simplex infection in a patient with early HIV infection.

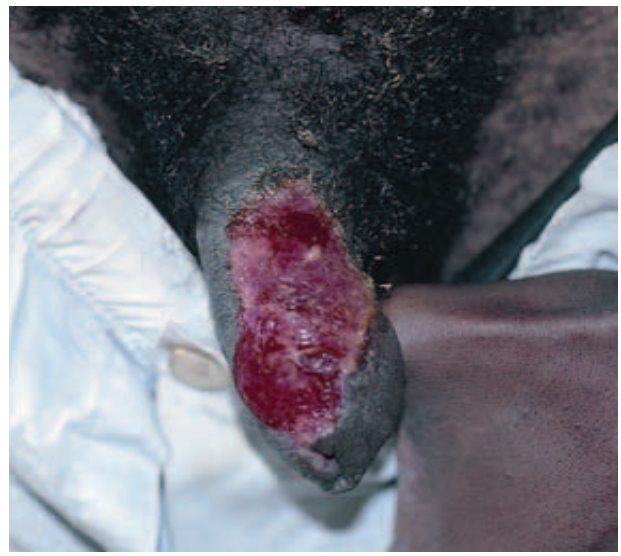

Fig. 2. Herpes simplex ulcerating penile lesions.

Variations in clinical manifestations can occur as a result of the location of the lesions. Genital HSV infection can manifest as oedema, ulcers, crusts, fissures, erythematous

patches, pustules or fleeting irritations. HSV infection in the anal region may resemble a traumatic lesion, while inguinal crease lesions can result in 'kissing' or adjacent lesions. Virtually all patients who have had symptomatic primary genital disease caused by HSV 2 will experience both symptomatic recurrence and asymptomatic shedding. However, no matter what the viral type and how infrequent the recurrences, asymptomatic viral shedding is a feature of HSV disease. Physicians are therefore obliged to warn patients of these facts and to advise appropriate prophylactic measures. The lower the CD4 cell count the greater the likelihood of shedding.

HSV infection is treated with aciclovir 400 mg tid, famciclovir 125 mg bid or valaciclovir 500 mg bid for 5 - 14 days. Recurrences are common, but prophylactic therapy is discouraged as the condition is not life-threatening and resistant strains which are very difficult to treat may develop after prolonged prophylaxis. If suppressive therapy is required, aciclovir 200 - 400 mg bid for up to 1 year has been advocated in cases with very frequent relapses. Early administration, preferably in the prodromal phase, is critical and maximises the value of treatment.

Cytomegalovirus can induce lesions similar to HSV and skin biopsy may be necessary to differentiate between the two conditions.

Foscarnet and cidofovir are administered intravenously for infections caused by aciclovir-resistant HSV. Imiquimod 5% cream has been used as topical treatment for cutaneous herpetic infections including those caused by aciclovir-resistant HSV strains.

VARICELLA ZOSTER VIRUS (VZV)

Herpes zoster (shingles)

Varicella zoster virus causes herpes zoster or shingles. Primary VZV infection presents as chickenpox, usually in childhood, and can then reactivate as herpes zoster in later life. HIV-related zoster may be recurrent, haemorrhagic, multidermatomal, disseminated or ulcerated (Fig. 3).

The head, neck and trunk are commonly affected. The initial extent and severity of the herpes zoster infection, severity of pain, and cranial (Fig. 4) and cervical dermatomal involvement are often associated with a poorer outcome.

Disseminated herpes zoster (Fig. 5), defined as cutaneous involvement of more than three contiguous dermatomes, more than 20 lesions scattered outside the initial dermatome or systemic infection (hepatitis, encephalitis, pneumonitis), may also develop more commonly in immunosuppressed patients.

Latent VZV infection can present with a clinical pattern of scattered vesicles in the absence of dermatomal herpes zoster.

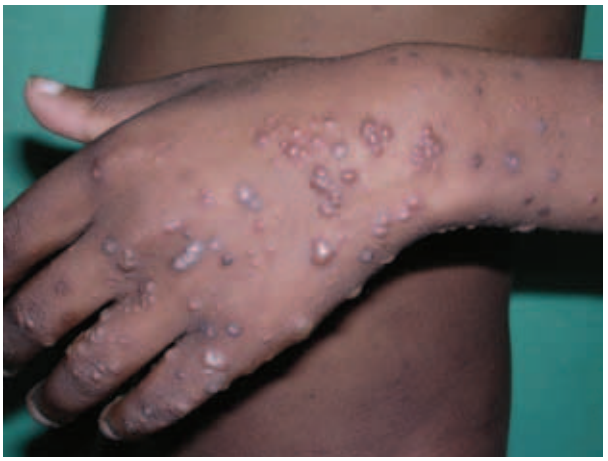

Fig. 3. Herpes zoster.

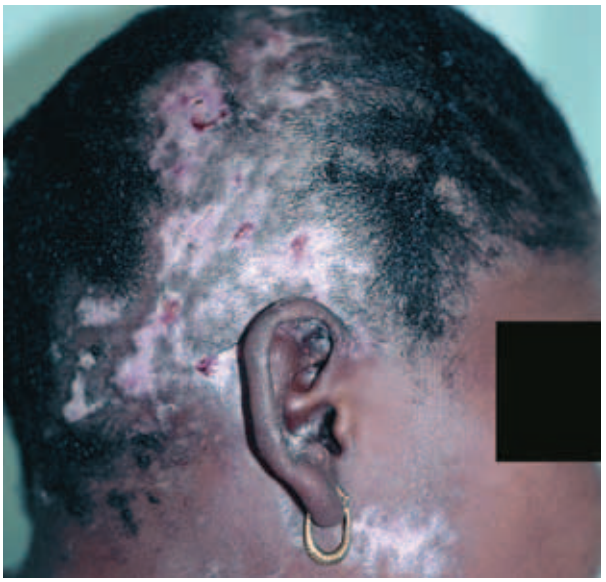

Fig. 4. Post-herpetic scarring (PHN).

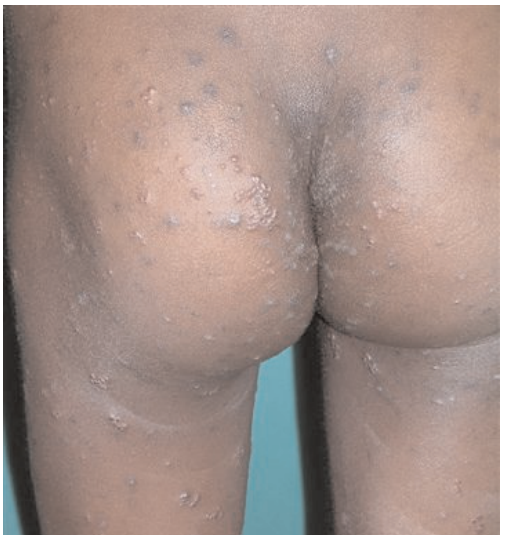

Fig. 5. Disseminated zoster.

Treatment with oral antivirals within 72 hours (or if lesions have been present for more than 72 hours, in the presence of new active lesions) is usually effective. Early treatment accelerates healing of skin lesions, decreases the duration of acute pain and may decrease the frequency of post-herpetic neuralgia (PHN).

Treatment is with aciclovir 800 mg po 5 times a day for 7 days or valaciclovir 1 g 3 times a day for 7 days or famciclovir 500 mg three times a day for seven days. The lesions are painful and attention should be given to adequate analgesia, e.g. paracetamol-codeine. Stronger analgesics may be required for the acute attack but should be avoided later.

It is important to look out for PHN, which is a common complication of HIV-related zoster and manifests as pain in the area of the lesions once they have cleared. It should be treated with analgesics with or without amitryptiline nocturnally.

VARICELLA (CHICKENPOX)

In chickenpox, the rash presents as a vesicular eruption on an erythematous base which may become pustular and crusted (Fig. 6). The rash tends to involve the face and trunk more than the limbs. In HIV it tends to become more dense and more extensive, may ulcerate and may involve systemic organs. Chickenpox may be confused with disseminated HSV infection or disseminated zoster. Especially in children, it may be an extensive mucocutaneous disease with repeated new crops of vesicles, which may necrotise and become haemorrhagic. If left untreated this has a high mortality in immune-suppressed individuals. Even though the diagnosis is usually made on clinical findings alone, when in doubt isolation of virus on viral culture from vesicular skin lesions confirms the diagnosis. Cytological examination of fluid or scraping from the base of a vesicle or pustule (tzanck smear) shows both giant and multinucleated epidermal cells, but cannot differentiate from herpes zoster or HSV infection. The following complications may occur and are seen more frequently in immunocompromised individuals: hepatitis, pneumonitis, encephalitis, and less commonly arthritis, carditis, nephritis and orchitis.

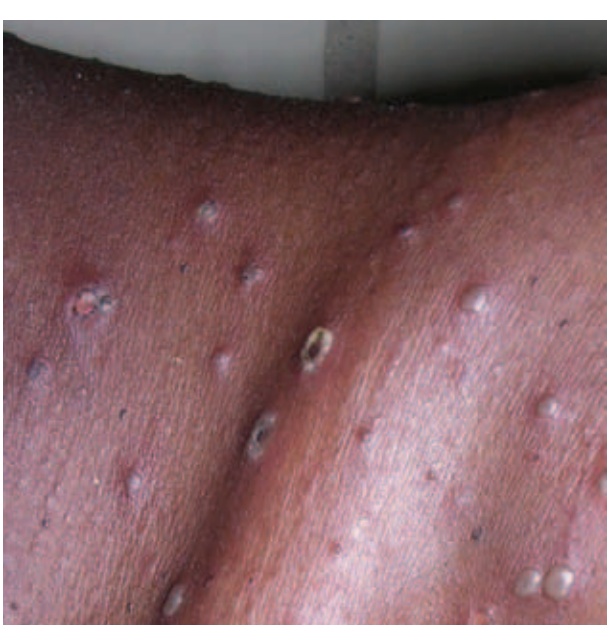

Fig. 6. Chickenpox.

Varicella-zoster immunoglobulin may reduce the severity of chickenpox if given within 72 hours of exposure. Oral aciclovir, valaciclovir or famciclovir are effective and may reduce the severity of the infection and recurrence. Symptomatic treatment of pruritus can be achieved with the use of systemic antihistamines. Treatment of bacterial secondary skin infection with the use of antibiotics may be required. Secondary bacterial infections such as staphylococcal pneumonia can be life threatening. Disseminated varicella in the immunocompromised host is treated with intravenous acyclovir.

MOLLUSCUM CONTAGIOSUM

Molluscum contagiosum is a common infection in HIV and typically presents with umbilicated flash-coloured, dome-shaped lesions (Fig. 7). In most cases molluscum contagiosum is self-limiting, and in adults it is most often sexually transmitted. It is seen more frequently in the paediatric population. In AIDS patients, molluscum contagiosum lesions can be widespread, attain immense size (giant molluscum) (Fig. 8) and have unusual locations.

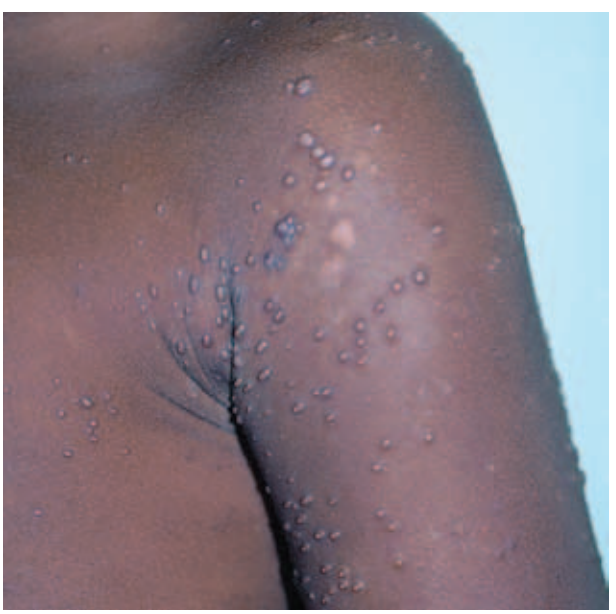

Fig. 7. Molluscum contagiosum.

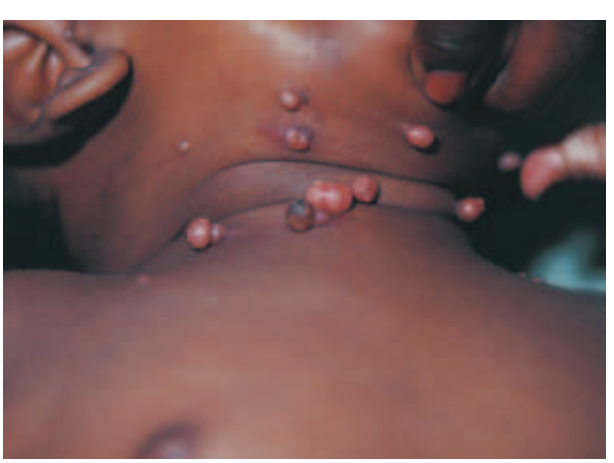

Fig. 8. Giant molluscum contagiosum.

The extent and size of the lesions is often related to the degree of immune compromise. In HIV-infected individuals it tends to be progressive and recurrent and very recalcitrant to therapy. Local treatment includes potassium hydroxide, silver nitrate, trichloroacetic acid or liquid nitrogen. Patients may need repeated applications. Cryotherapy, electrocautery and imiquimod 5% cream may be tried though the latter is expensive. There is often complete resolution of lesions in those patients who recieve HAART. Diagnosis can be confirmed by biopsy, and if there is reason to suspect another diagnosis, the specimen can be sent for fungal culture and histology. In more severely immune suppressed individuals, the differential diagnosis includes cryptococcosis and histoplasmosis. Systemic illness associated with variable morphology of lesions should alert the clinician.

CYTOMEGALOVIRUS

Although ulcers can occur anywhere, lesions are commonly seen as perianal ulceration (Fig. 9) and may be mistaken for genital herpes ulceration. The most common sites of infection are adrenal gland (75%), lungs (58%), gastrointestinal tract (30%), and central nervous system (20%). Biopsy of the skin lesion for histology and culture will help to differentiate it from HSV.

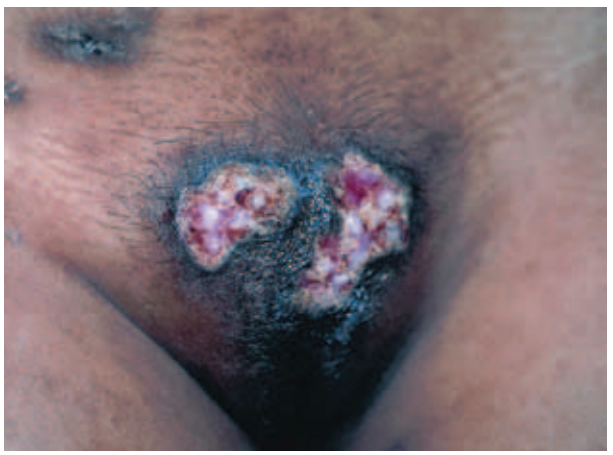

Fig. 9. Cytomegalovirus.

Fig. 10. Verruca vulgaris.

HUMAN PAPILLOMAVIRUS INFECTIONS

Verruca vulgaris

Human papillomaviruses commonly produce skin lesions during the course of HIV disease. In contrast to other opportunistic viral infections, the incidence of HPV

Fig. 11. Verruca planar (epidermodysplasia verruciformis-like lesions, face).

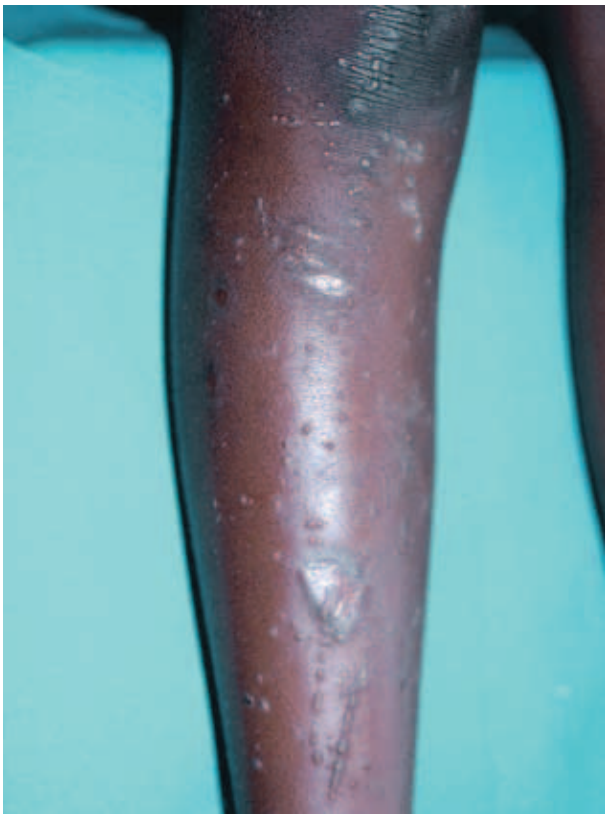

Fig. 12. Verruca planar (epidermodysplasia verruciformis-like lesions, shins).

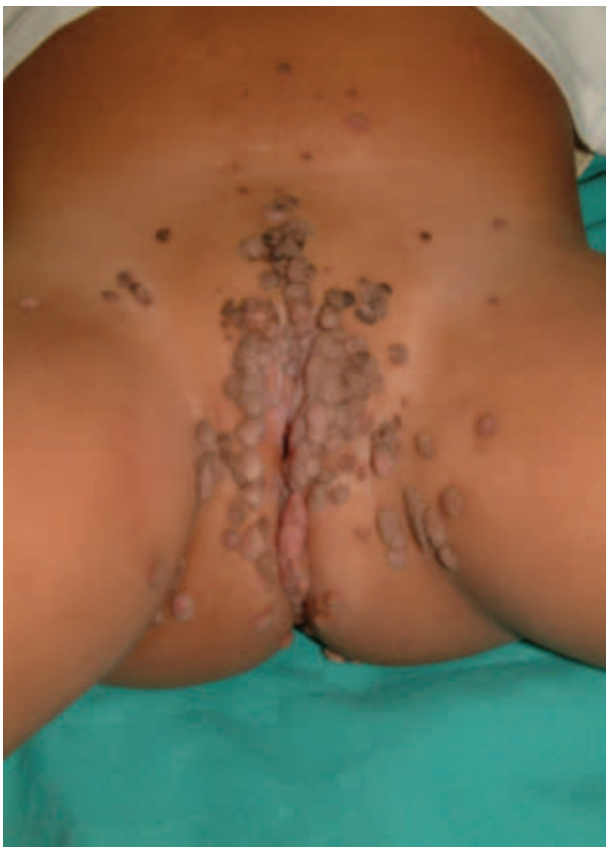

Fig. 13. Condyloma acuminatum.

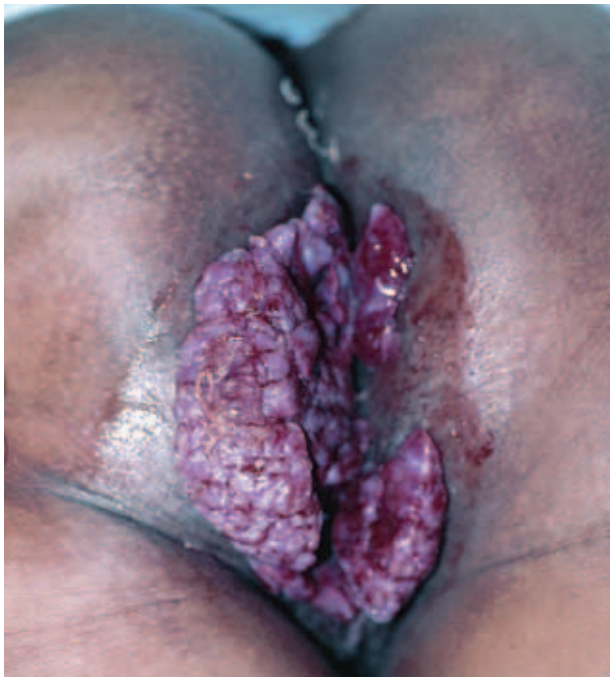

Fig. 14. Condyloma acuminatum.

infections may actually increase despite patients being on HAART. A variety of skin lesions may be seen, ranging from verruca vulgaris (Fig. 10), which can enlarge and become confluent, to an unusual pattern of extensive verruca plana and pityriasis versicolor-like warts which may resemble epidermodysplasia verruciformis (Figs 11 and 12). These lesions tend to be unresponsive to therapy. Treatment modalities include use of cryotherapy, electrocautery, surgical excision and use of imiquimod.

Genital warts

HPV 6 and 11 tend to infect mucosal areas causing condylomata acuminata, which can be large (Figs 13 and 14). In the immune-compromised individual condylomas are more common, more extensive and resistant to treatment. They are often associated with vulvar intraepithelial neoplasia and squamous carcinoma, and cervical and anal intraepithelial neoplasia. Diagnosis is usually made by recognition but biopsies should be performed if lesions look atypical, or if the warts are resistant to conventional treatment or become hyperpigmented, indurated, fixed or ulcerated. Apply podophyllin 25% to anogenital warts weekly (not in pregnancy). Wash off after 4 hours to prevent irritation. Alternatively apply 80% trichloroacetic acid in water weekly. Cautery, liquid nitrogen or laser therapy may be required but recurrences do occur.

ERRATUM

Part 1 of the article 'Cutaneous manifestations of HIV/AIDS', which appeared on pp. 12 - 17 of the November 2004 issue of the *Southern African Journal of HIV Medicine*, contained a sentence that could be misleading. On p. 15 (left-hand column) the dosage of amphotericin B for treating the acute stage of histoplasmosis is given as 15 mg/kg. The dosage is in fact 0.7 mg/kg/d.

In response to a reader query, the authors have also clarified the dosage of fluconazole. On p. 13 (right-hand column) it was stated that when oesophageal candidiasis is suspected, fluconazole 100 mg/d should be given for 5 days. The treatment for oral candidiasis that is not responsive to topical treatments is 100 mg fluconazole once per day. If oesophageal candidiasis is suspected (dysphagia with oral candida) the dosage is 200 mg fluconazole daily for 2 - 3 weeks.