PART I: PAEDIATRIC HIV DERMATOSES

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Introduction

Human immune deficiency virus (HIV) infection can affect multiple organs, including the skin. The skin is the largest and most visible organ in the body. Skin manifestations (dermatoses) of HIV infection are variable and many HIV-associated skin conditions are often more severe and associated with worse morbidity than in HIV uninfected persons.

Infections due to fungi, bacteria and viruses, as well as infestations are either more common or more severe in this population. These infections and infestations also tend to have atypical presentations, are usually more recurrent and less responsive to conventional therapy compared to healthy children. Some malignancies, particularly haematological, inflammatory and drug-associated dermatoses are also more common. Cutaneous manifestations of nutritional deficiencies are also commonly seen in HIV-infected children.

A correlation between skin disease and underlying immune suppression has been reported in several studies, making the diagnosis of skin disease a valuable tool in the prediction of HIV infection and staging thereof.

With the increasingly early use of antiretroviral therapy (ART), there has been a decline in the incidence and prevalence of HIV-associated skin disease.

The skin is an active immune organ and contains antigen presenting cells like Langerhans and dermal dendritic cells, as well as other cells and cytokines that are involved in both the innate and acquired immunity. In AIDS, the antigen presenting cells, many of which are CD4+, are depleted together with CD4+ T cells, natural killer cells, macrophages and monocytes. These cells are usually the first line of defence, as the skin is exposed to a wide variety of pathogens and in the deficiency of this first line of defence, antigen presentation, granuloma formation and cytotoxic capabilities in the skin are markedly impaired. This results in diminished control of infections and impaired inflammatory responses. Poor control of viral infections can also be associated with uncontrolled cell replication and increased potential for malignant transformation.

The impairment of the cutaneous immune responses, which may be present early in the course of HIV-1 disease, is believed to be responsible for the high incidence of both infectious and non-infectious dermatoses, even before the development of full immunodeficiency. Fifty to eighty per cent of ART naïve children are reported to have at least one skin manifestation of HIV, prevalence being highest in those with severe immunosuppression.

Further reading

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CHAPTER 1: BACTERIAL INFECTIONS

Staphylococcal Infections

A high percentage of HIV-infected persons are nasal carriers of *Staphylococcus aureus*, hence the high rate of infection in this population.

Impetigo

Description: Impetigo is a superficial bacterial skin infection characterised by flaccid pustules and honey-coloured crust. It usually begins as a small painful erythematous papule.

Aetiology: The most common implicated organism is *Staphylococcus aureus*, although group A beta-hemolytic streptococcus (*Streptococcus pyogenes*) has been implicated in some cases.

Clinical presentation: Impetigo can be bullous and non-bullous, usually on the face and extremities. Primary impetigo presents as erythematous plaques with or without thin-walled vesicles that break down leaving characteristic yellow crust. Secondary impetigo can occur in other dermatoses e.g. eczema.

Epidemiology: Impetigo is common in children especially those aged 2-5 years and prevalence of 15 - 25% has been reported in the tropics. It is transmitted by contact with infected skin.

Diagnosis: Diagnosis is usually clinical but a Gram stain and culture may be required to confirm diagnosis when there is extensive disease.

Treatment: This should be guided by local antibiotics sensitivity testing but in mild and localized infection, first-line topical antibiotics like mupirocin, bacitracin or fusidic acid for 7-10 days are effective. If the infection is widespread, severe or is associated with lymphadenopathy, oral penicillins (flucloxacillin) or macrolides (erythromycin) if patient is allergic to penicillins, are indicated for 7-10 days. Parenteral antibiotics may be required if impetigo is diagnosed in a very sick child.

Complications: Cellulitis, osteomyelitis, staphylococcal scalded skin syndrome, and acute post-streptococcal glomerulonephritis can occur.

Prevention: Regular care of healthy skin and minimal skin contact with an infected child reduces the risk of transmission. Prompt diagnosis and treatment will prevent complications. In settings where impetigo is endemic among children, measures to reduce the transmission frequency should be adopted, including encouraging regular hand washing, educating the population on health matters and instituting treatment early in the course of the disease.

Further reading

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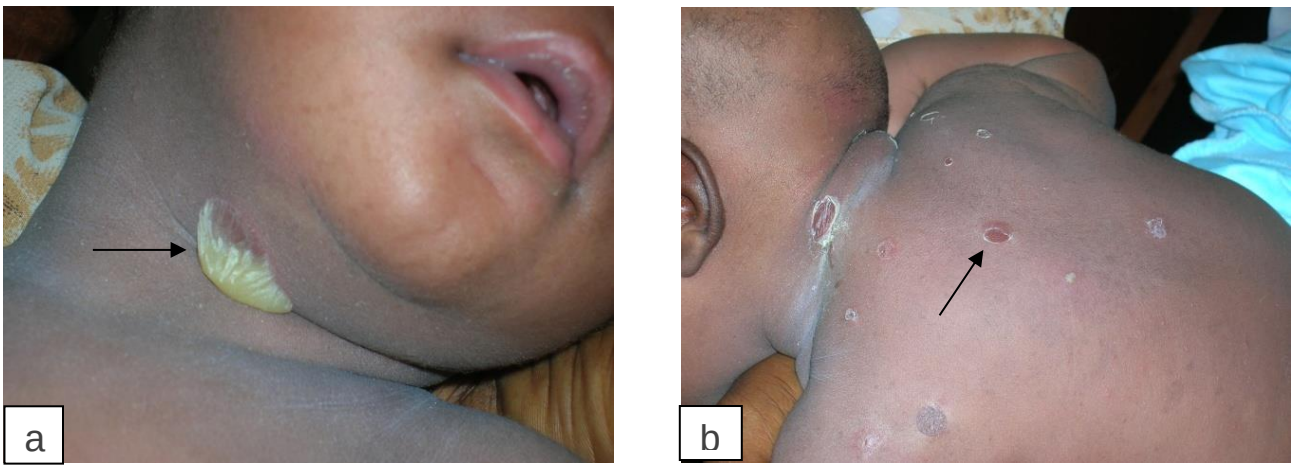

Figure 1 a and b: Bullous impetigo in a 2-month-old HIV-exposed infant. Note the flaccid pustule (left) and the older ruptured lesions (right).

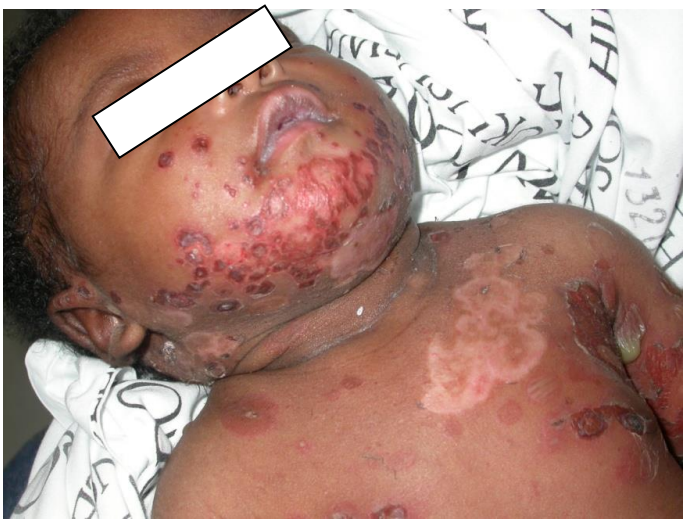

Figure 2: Bullous impetigo in a 3-month-old child. Note the lesion in different stages of evolution ranging from intact blisters, ruptured blisters and post-inflammatory hypopigmentation of healed lesions

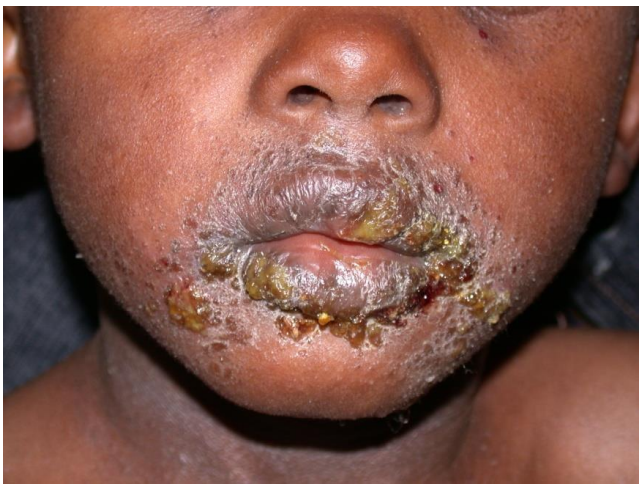

Figure 3: A child with secondarily impetiginised atopic eczema periorally.

Folliculitis

Description: Folliculitis is the inflammation of the hair follicle. It can be caused by physical injury, chemical irritation or an infection.

Aetiology: *Staphylococcus aureus* is the most frequent cause of infective folliculitis but folliculitis can also be caused by pathogenic fungi *e.g. Candida albicans*, commensal fungi such as *Malassezia furfur* and mites such as *Demodex* species. These are most often seen on the face in immunosuppressed children.

Clinical presentation: The presentation may be in the form of itchy, painless or painful papules, dome-shaped pustules (with hair shaft at the centre) often with an erythematous base. Folliculitis has predilection for the scalp, extremities, occluded areas and areas prone to excessive moisture and chafing. Systemic symptoms are not common.

Epidemiology: It is a common bacterial skin infection in childhood.

Diagnosis: It is a clinical diagnosis, but Gram stain and culture of pus may be required to confirm diagnosis.

Prevention: Prompt diagnosis and treatment reduces spread of the disease. Regular care of healthy skin reduces infection rates will prevent complications. Treatment of *Staphylococcus* carriers, particularly caregivers of affected children is important in reducing transmission and recurrence. Those who participate in sports should shower regularly and not share personal clothing.

Treatment: Mild staphylococcal folliculitis is often self-limiting, or may respond to cleansing or topical antiseptics. In more severe cases, antibiotics, topical or systemic, may be required. Topical mupirocin may suffice for mild infection. For deep-seated infection, oral antibiotics should include coverage for S. aureus, such as penicillinase-resistant penicillins e.g. flucloxacillin or macrolides – e.g. erythromycin. First-generation cephalosporins such as cephalexin may also be used.

If the infection is persistent or recurrent, the usual sites of staphylococcal carriage should be sought in the patient, contacts or caregivers and anti-staphylococcal measures initiated. Application of ½ strength hibitane cream or mupirocin cream to nostrils twice daily for 5 days is indicated. This has to be repeated monthly as re-colonization is common.

Complications: These include furuncles, carbuncles, septicaemia and osteomyelitis all of which may be recurrent.

Further reading

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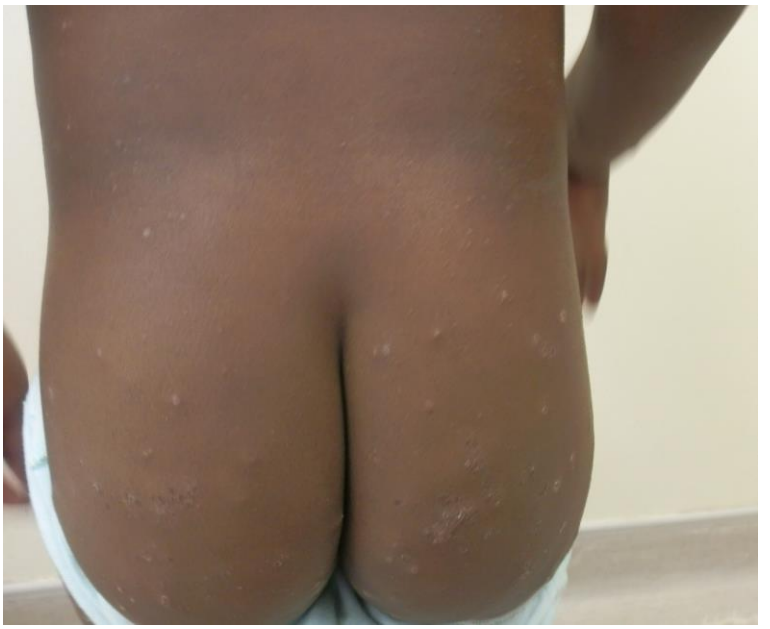

Figure 4: Folliculitis in a child. Note multiple papules and pustules on the buttocks, trunk and thighs.

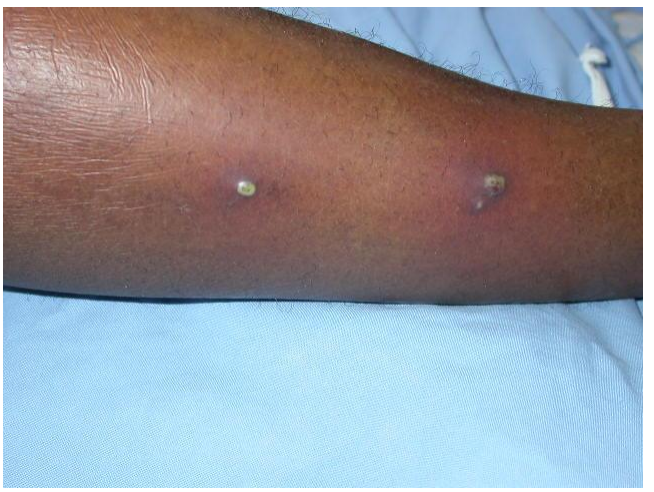

Figure 5: Folliculitis on the leg. Note the pustules and surrounding erythema. Folliculitis is often a precursor to furuncles and carbuncles.

Furunculosis

Description: Furunculosis (boil or abscess) is inflammation of the hair follicle with small abscess formation extending through the dermis into the subcutaneous layers. When furuncles aggregate to form broad, swollen, erythematous, deep, and painful masses that usually open and drain through multiple tracts they are called carbuncles.

Aetiology: Furunculosis is suppurative sequelae of a folliculitis. *Staphylococcus aureus* is the primary aetiological agent.

Clinical presentation: A furuncle appears as a red tender, firm, erythematous, often fluctuant nodule on hair-bearing parts of the body, with central purulence that may spontaneously drain. They are most often seen on the neck, face, buttocks, axillae, and groin.

Epidemiology: It is transmitted by contact with infected skin and other fomites. It is often spread to other family members. Predisposing factors include poor hygiene, overcrowding, immunodeficiency and malnutrition.

Diagnosis: Clinical but Gram stain and culture of pus may be required to confirm diagnosis.

Prevention: Family hygiene including regular hand washing, fomite cleaning, and avoiding contact with contaminated skin. In recurrent cases effort should be made to exclude diabetes and other causes of immunosuppression. Nasal and perineal carriage of *Staphylococcus aureus* in the patient and other household members should be sought and treated.

Treatment: May resolve spontaneously, but surgical drainage of pus is mainstay of therapy. If surrounding cellulitis or systemically unwell, cloxacillin IV 25 – 50 mg/Kg/dose 6 hourly or flucloxacillin PO may be indicated. Treatment of recurrent furunculosis involves therapeutic triad of antibiotics, decolonisation and decontamination.

Complications: These include carbuncles, septicaemia, osteomyelitis and scarring.

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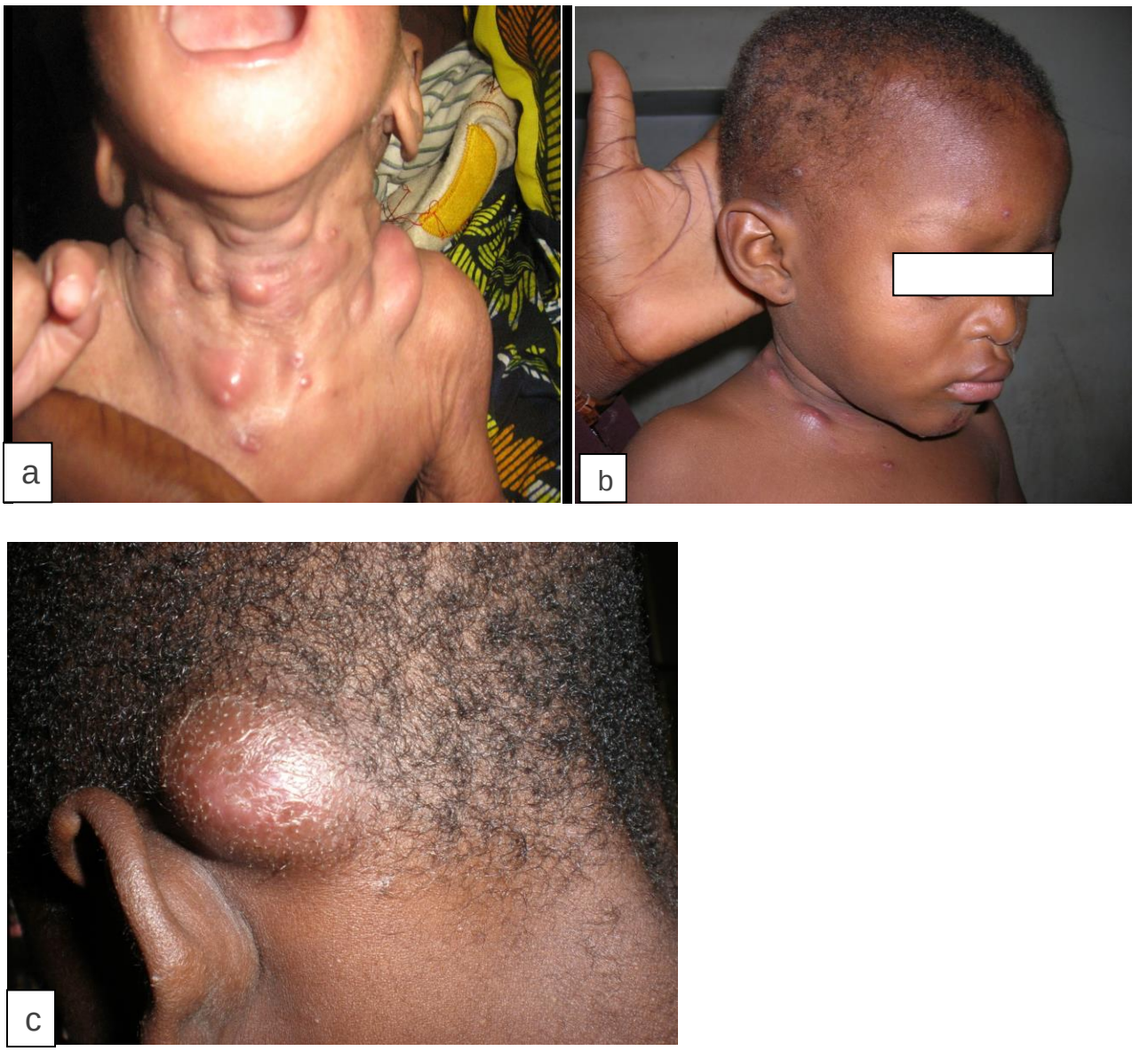

Figure 6a, b and c: Pictures showing a combination of furuncles and carbuncles in immunosuppressed children, multiple fluctuant erythrematous nodules, on neck (a), face and scalp (b), postauricular (c).

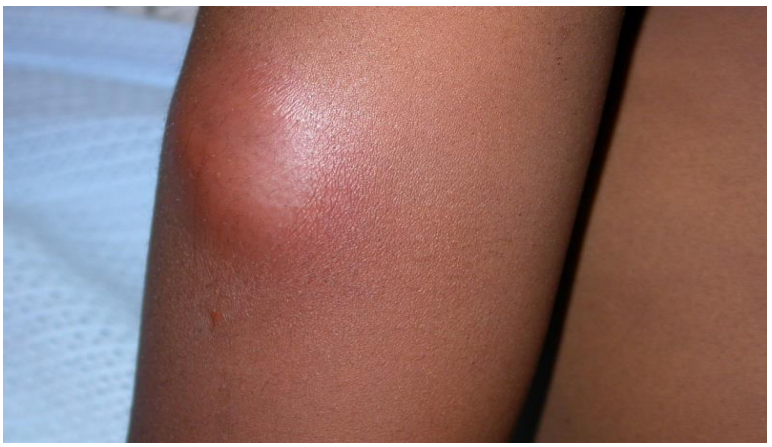

Figure 7: Another picture of a carbuncle presenting as a red nodular swelling on the upper arm.

Necrotising Fasciitis (NF)

Definition: An acute bacterial infection (also known as "flesh eating bacteria") that is characterized by necrosis of the deep fascia and subcutaneous tissues. It is a progressive and rapidly spreading infection in the deep tissue planes.

Aetiology: NF can be classified as polymicrobial (type I) or monomicrobial (type II), type I being more common. Type I NF is caused mainly by a combination of Group A *Streptococcus* (most common), *Klebsiella*, *Clostridium*, *E. coli*, *Staphylococcus aureus,* and *Aeromonas hydrophila.*

Clinical presentation: Pain, swelling and redness at the site of infection, followed by frank necrosis within days or weeks. Constitutional symptoms and signs such as fever, tachycardia and tachypnoea may be present. Presence of crepitus indicates gas produced by aerobic and anaerobic organisms is considered diagnostic of NF, but together with haemorrhagic bullae, skin necrosis, crepitus, sensory and motor deficits, it is a late sign of NF.

Epidemiology: Most common in immunocompromised hosts such as patients with HIV infection and diabetics.

Diagnosis: NF is a clinical diagnosis and Gram stain, blood and tissue cultures aid management.

Treatment: Surgical debridement, fasciotomy and broad spectrum intravenous antibiotics are the mainstay of treatment. Initial antibiotic treatment could include penicillin G and an aminoglycoside. Clindamycin may be added to cover streptococci, staphylococci, gram-negative bacilli, and anaerobes. Antibiotics are adjusted with culture results.

Complications: NF has a high mortality and other complications include necrotizing myositis, septic shock and multiple organ failure.

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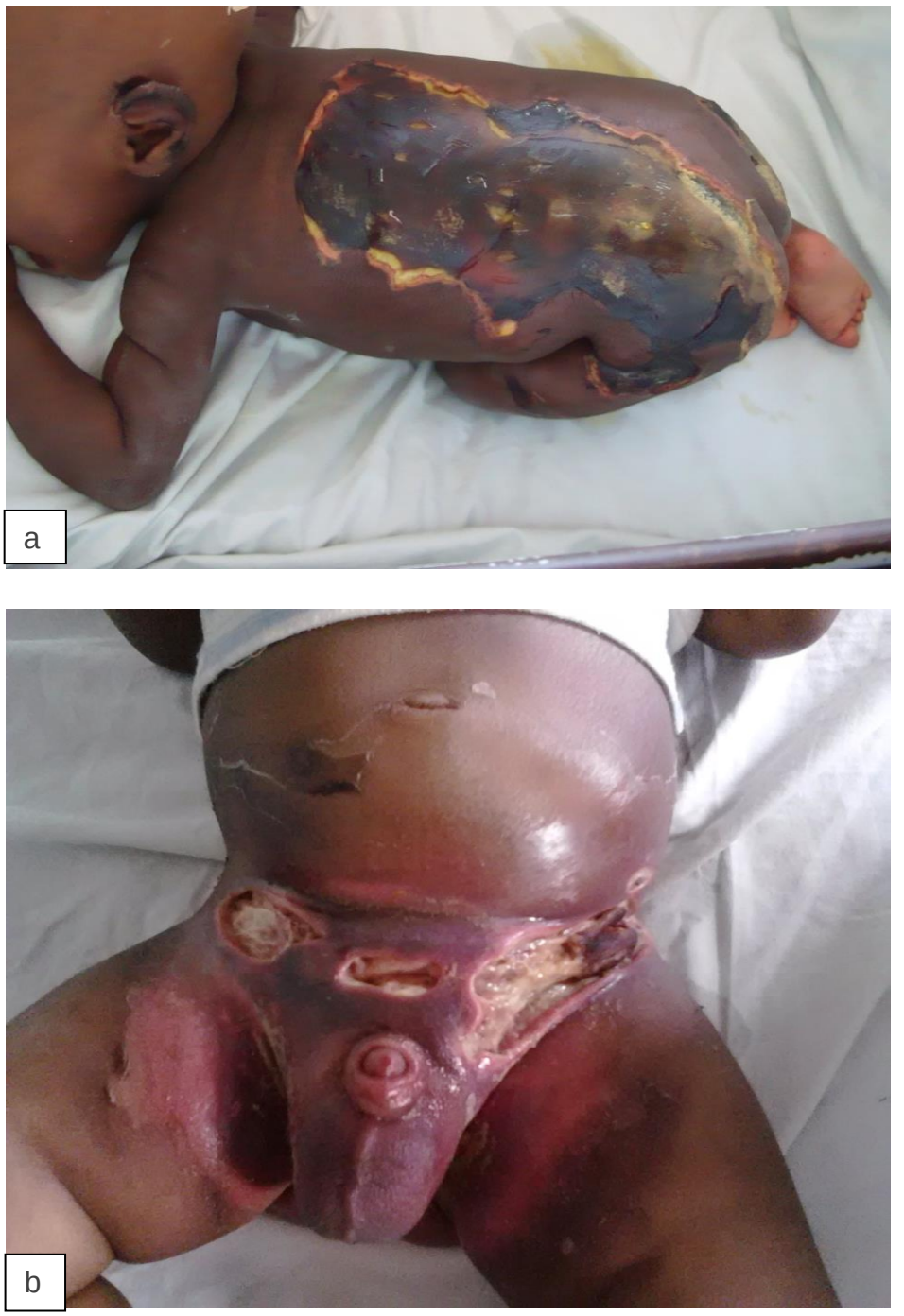

Figure 8a and b: Necrotizing fasciitis

Ecthyma Gangrenosum

Definition: Ecthyma gangrenosum is a cutaneous infection usually caused by *Pseudomonas aeruginosa.*

Aetiology: It is usually a manifestation of bacterial systemic infection with *P. aeruginosa* in immunosuppressed persons, including those with AIDS, diabetes mellitus and neutropenia.

Clinical presentation: Characteristically presents as tender pustules or haemorrhagic blisters with an erythematous edge that progress to form a central black eschar and ulcerate.

Epidemiology: Ecthyma gangrenosum is rare.

Diagnosis: Ecthyma gangrenosum is a clinical diagnosis and suspicion of the disease warrants a prompt tissue and blood cultures.

Prevention: Maintenance of personal hygiene and care of open wounds in immunosuppressed persons.

Treatment: On clinical suspicion, broad-spectrum empiric antibiotic therapy to include anti-pseudomonal coverage should be initiated. Options include aminoglycosides, fluoroquinolones e.g. ciprofloxacin or third-generation cephalosporins e.g. ceftazidime/ceftriazone. If the lesions fail to respond to antibiotics, surgical debridement may be required.

Further reading

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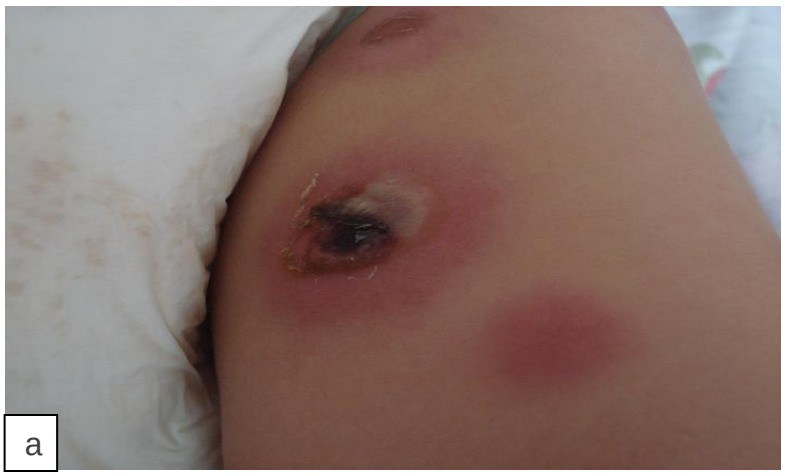

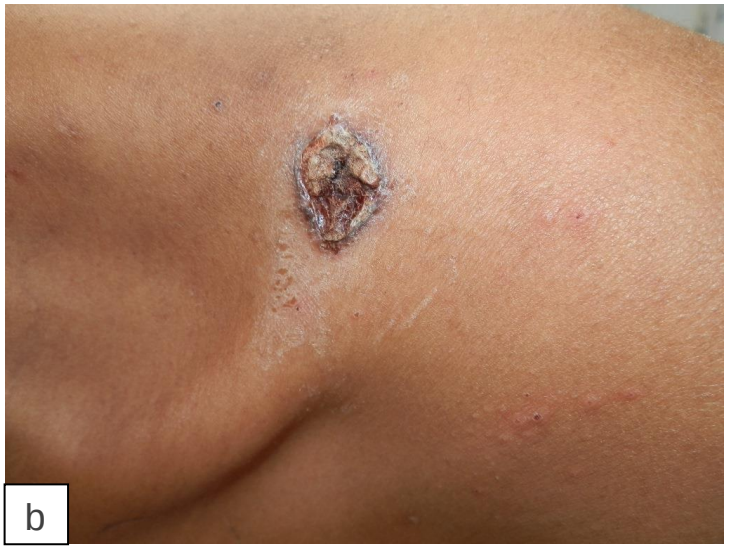

Figure 9a and b: Necrotic ulcers in ecthyma gangrenosum with an erythematous rim in (a) Differential diagnosis includes other lesions presenting with a black necrotic centre (eschar) – cutaneous anthrax, cutaneous aspergillosis, rickettsia and cutaneous leishmaniasis

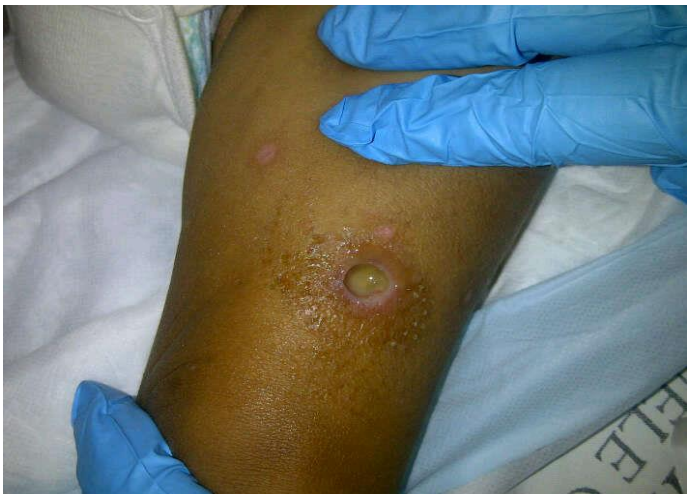

Figure 10: Ecthyma gangrenosum: showing a lesion at a late stage of evolution.

Table 1: Treatment options: Bacterial Infections

Bacterial Infections	**1st line therapy**		**Alternative therapy**
Impetigo	Topical therapy	Mupirocin	Fusidic acid
	Systematic antibiotics	Flucloxacillin, IV cloxacillin	Macrolides e.g. Erythromycin
Folliculitis	Topical therapy	Mupirocin	Macrolides
	Systematic antibiotics	Flucloxacillin	Erythromycin, Cephalexin
Furunculosis	As for folliculitis		
Necrotising Fasciiitis	IV penicillin G, gentamycin and clindamycin	Fasciotomy as required	
Ecthyma gangrenosum	Ciprofloxacin, ceftazidime		

Cutaneous Tuberculosis (TB)

Definition: This refers to either invasion of the skin and mucous membranes with *Mycobacterium tuberculosis* or a hypersensitivity reaction to the organism.

Aetiology: *M. tuberculosis* can infect the skin and the route of infection and immune status of the person influences clinical presentation. Tuberculids and erythema induratum are hypersensitivity reactions usually seen in people with good immunity.

Clinical Presentations

- Tuberculids – typical lesions are small, erythematous papules that become pustules and undergo central ulceration and heal spontaneously within weeks, leaving a varioliform scar. The lesions develop symmetrically over the extensor surfaces, particularly the knees, the elbows, and the dorsum of the hands and the feet, although widespread involvement may be present.
- Tuberculids are thought to be an exaggerated host immunologic response to the mycobacteria or its antigens in the blood stream. As many as 40% of the patients may have accompanying active TB.
- Scrofuloderma – refers to direct extension of TB from underlying lymph nodes, bones or joints into the skin. Usually seen as firm painless nodule and ulcerate and heal with scarring.
- Lupus vulgaris – chronic progressive direct infection of the skin presenting as reddish-brown plaques with a jelly-like consistency.
- TB verrucosa cutis – results from direct inoculation of TB into the skin of a person who was previously infected with the bacteria. Presents as brownish-red wart-like growths.
- BCGitis – presents often as fever and regional lymphadenopathy sometimes becoming suppurative. However, in immunosuppressed persons, systemic dissemination of the attenuated *Mycobacterium bovis* vaccine can occur.
- Cutaneous TB immune reconstitution inflammatory syndrome – on initiation of antiretroviral therapy in HIV-infected persons, there may be a paradoxical worsening of any of the above-mentioned clinical presentations of cutaneous TB.
- Miliary TB – widespread seeding of *Mycobacterium* tuberculosis into internal organs and the skin via haematogenous spread. Miliary TB is so named because of a millet-like appearance of the TB bacilli in the lung, as seen on a chest x-ray. On the skin miliary TB most often presents as vesiculopapules, the size of a pinhead that become necrotic.

Epidemiology: Cutaneous TB is rare.

Diagnosis: Cutaneous TB is confirmed by a skin biopsy that shows characteristic features and a tissue culture.

Prevention: Vaccination, early detection, treatment and completion of the course are the mainstays of disease transmission in general. However, the risk of transmission in cutaneous TB is minimal.

Treatment: Six months standard intensive treatment with rifampicin, isoniazid, pyrazinamide and ethambutol for 2 months followed by the continuation phase with rifampicin and isoniazid is effective for cutaneous TB. However, in instances of severe or complicated disease it may be extended to nine months.

Complications: Miliary TB has a high mortality, scrofuloderma may be associated with severe scarring and contractures and lupus vulgaris may result in squamous cell carcinomas.

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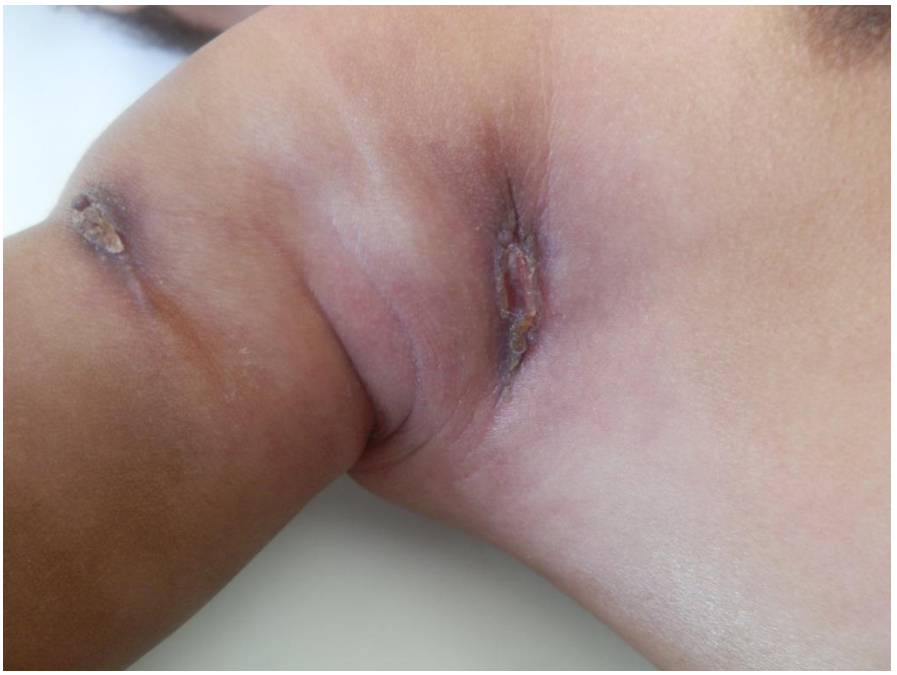

Figure 11: Scrofuloderma: Ulceration in the axilla and arm of an HIV-infected child with tuberculosis.

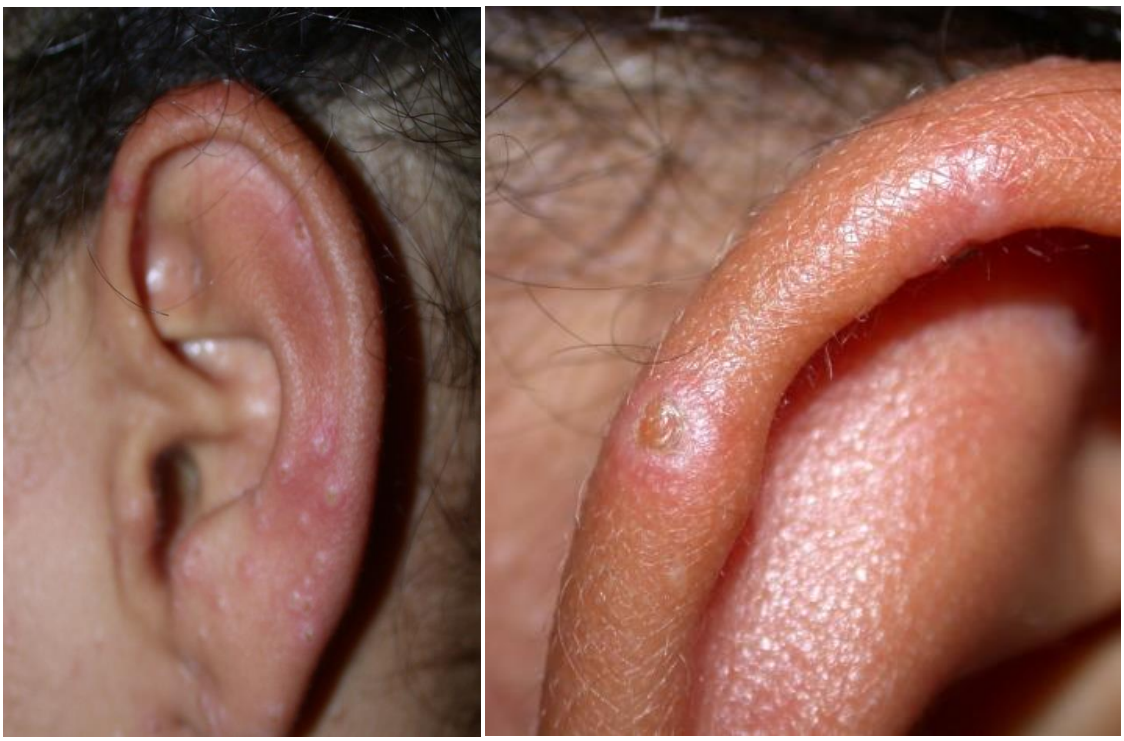

Figure 12: Papulonecrotic tuberculids on the ear of a child. Note the papules with central necrosis.

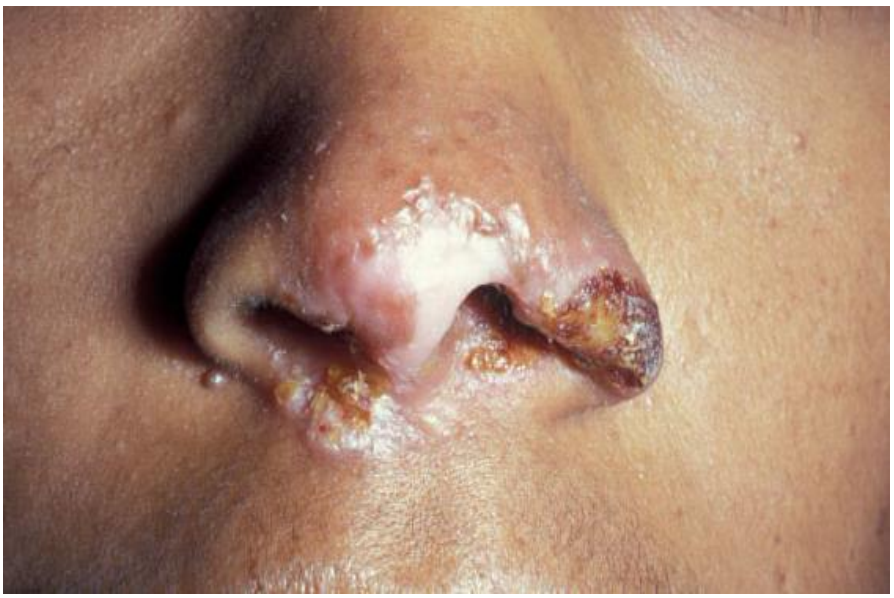

Figure 13: Lupus vulgaris on the nose of a patient with tuberculosis.

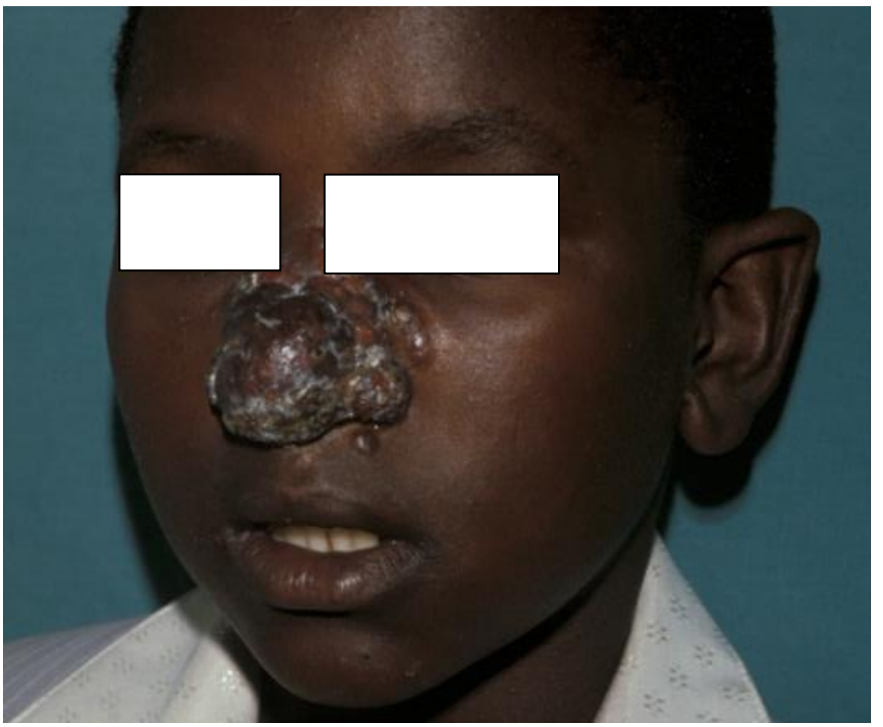

Figure 14: Large plaque and satellite nodules on the nose of a child with lupus vulgaris.

CHAPTER 2: VIRAL SKIN INFECTIONS

Herpes Simplex

Description: Herpes simplex viral (HSV) is a common, chronic or recurrent infection in the paediatric HIV population. The clinical presentation of HSV in HIV-infected patients is often atypical and standard therapy often ineffective. HSV infection should be suspected in any chronic vesicular or mucocutaneous ulceration disease and Tzank smear should be performed.

HSV usually affects both the buccal and genital mucosae, but in HIV can affect the skin.

Aetiology: Herpes simplex (HSV) type 1 causes oral lesions while type 2 affects genitalia. An infected mother can transmit the virus to her unborn child through exposure to infected maternal genital fluids.

Clinical presentation: HSV presents as orolabial painful blisters and/or punched out ulcers, which may be associated with fever, irritability and lymphadenopathy. In HIV, the ulcers are chronic and non-healing with rolled edges. A high index of suspicion is needed to make the diagnosis.

In neonates and immune-compromised individuals, it may present as disseminated disease and in this setting encephalitis is not uncommon.

Epidemiology: In any population and age group, HSV-1 is more common than HSV-2 and the prevalence of HSV-1 in non–high-risk populations increases in a linear fashion with age, with most initial infections occurring in childhood and adolescence. HSV-1 prevalence is > 40% in 15 year olds, before increasing to 60%–90% in adulthood. HSV-2 is prevalence is strongly associated with age, increasing from negligible levels in children < 12 years to as high as 80% amongst older higher risk populations.

Diagnosis: In uncomplicated cases, the diagnosis is mainly clinical, but a Tzanck smear, viral culture, PCR technique is helpful in atypical cases including CSF PCR or culture in suspected encephalitis.

Prevention: HSV is transmitted most commonly during delivery, but also can be transmitted in utero or through postnatal contact with the mother or other caretakers. Prevention is therefore crucial, some specialists recommend prophylactic acyclovir therapy, some recommend routine caesarean section and others recommend both. However, for those who have a history of recurrent genital HSV, a recent review of best evidence found insufficient data to support the use of prophylactic acyclovir. Contact with infected vesicles should be avoided.

Treatment: The drug of choice for treating localised HSV infection in infants and children is acyclovir. The recommended dose is 20 mg/kg/day in five divided doses Xu-10 days. Usually if the child <2 years: acyclovir 100 mg 5 times a day for 10 days or 200 mg three times a day for 10 days.

If child >2 years: acyclovir 200mg 5 times a day for 10 days or 400 mg three times a day for 10 days. In case of acyclovir resistance or where available: Foscarnet 120-200 mg in two to three divided doses can be used.

Although commonly prescribed by many physicians, topical antiviral medications such as acyclovir ointment are not recommended to treat most mucocutaneous HSV lesions because such therapy does not reduce the severity or duration of infections in immunocompetent hosts. Topical therapy can be used in immunocompromised patients to accelerate the healing of lesions.

Complications: Dissemination, concomitant infection with other pathogens including viruses, such as CMV, yeasts infection (Candida) or secondary bacteria may occur. Potential risk of developing HPV associated epithelial neoplasia exists.

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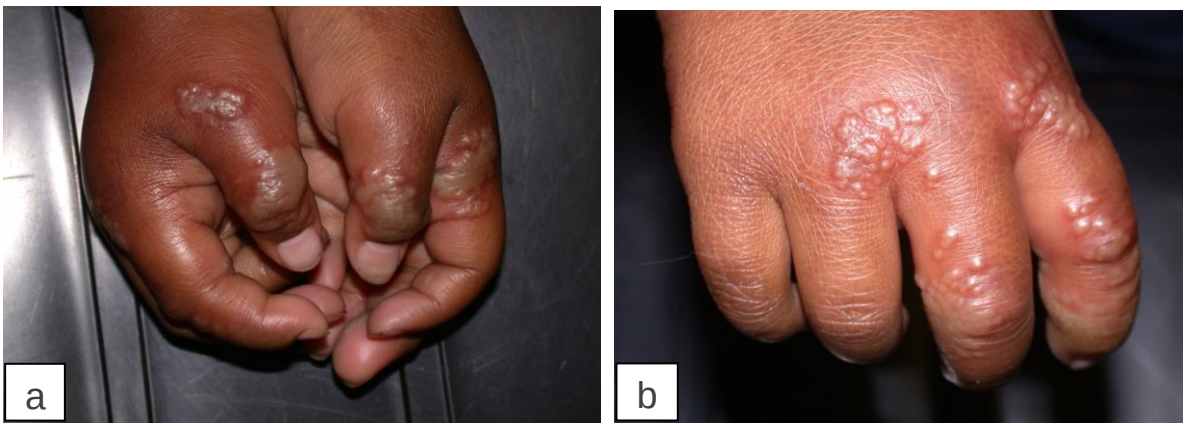

Figure 15a and b: Multiple grouped vesicles on the hand of a child with herpes simplex infection.

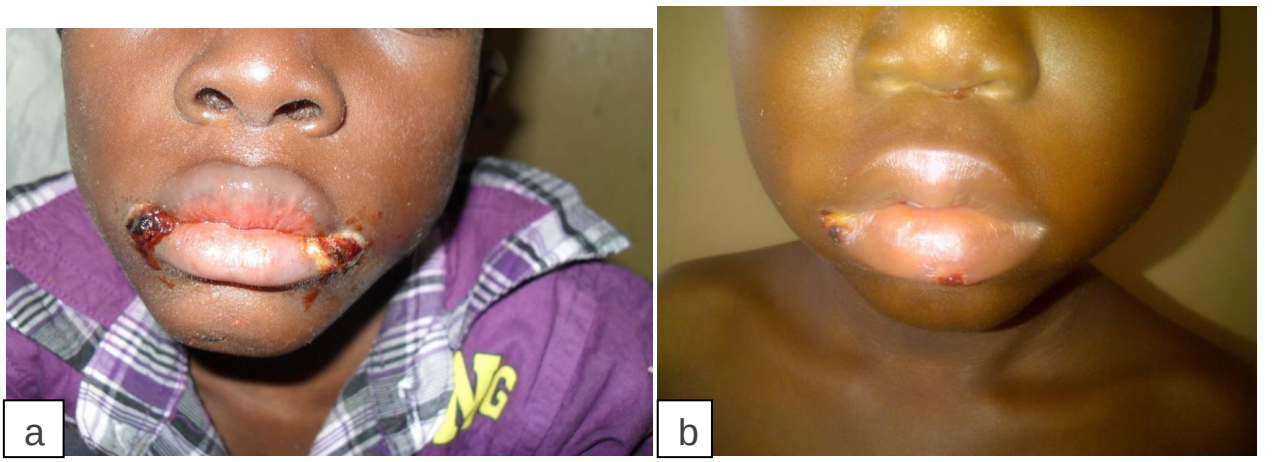

Figure 16a and b: Angular stomatitis in children with herpes simplex. Note the involvement of the columella in (b)

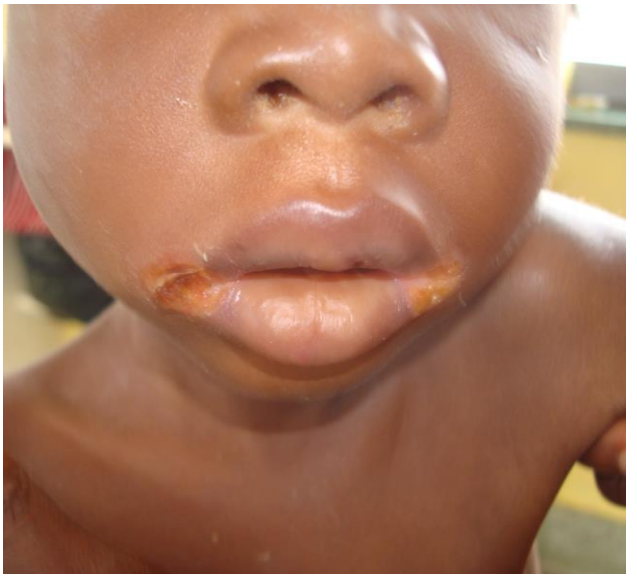

Figure 17: Herpes simplex lesions with angular stomatitis and possible secondary bacterial infection.

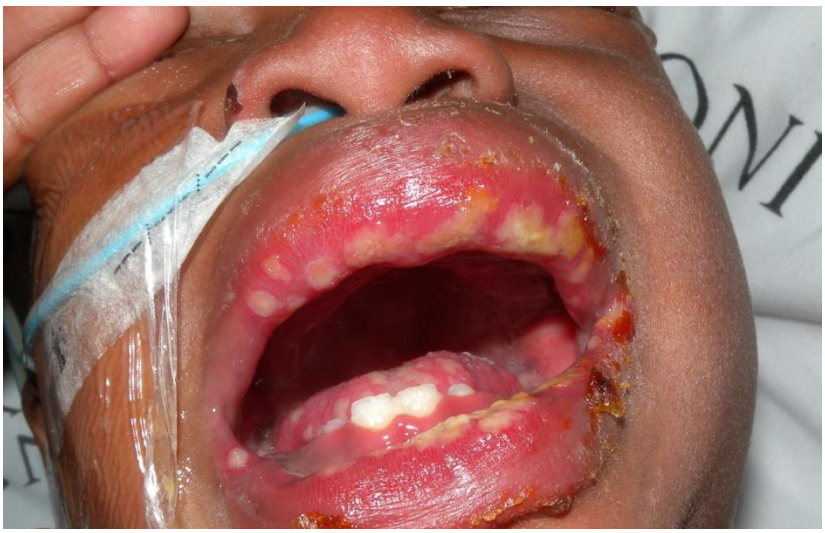

Figure 18: Herpes simplex in an immunocompromised child affecting the lips, angle of the mouth and the tongue

Eczema herpeticum

Patients with atopic dermatitis are susceptible to acute generalised infections with herpes simplex virus, referred to as eczema herpeticum. Eczema herpeticum can be caused by either type 1 or type 2 HSV. Eczema herpeticum in immunocompromised children such as those who have HIV, tend to have higher risks of dissemination and longer durations of outbreaks and are less responsive to therapy.

Eczema herpeticum presents as monomorphic eruptions of dome-shaped vesicles that may transform into pustules. The vesicles dry out within 2 to 3 weeks and may leave erosive pits. These "punched out" erosions can create a scalloped appearance at the periphery of the large denuded area.

Eczema herpeticum is a clinical diagnosis and can be confirmed by a Tzanck smear, performed by unroofing a vesicle and scraping the base of a lesion. On light microscopic examination, multinucleated giant cells are seen. HSV culture, PCR or a direct fluorescent antibody test are other confirmatory tests. When a secondary infection is suspected, a bacterial culture is obtained.

Prevention: Parents of children with moderate to severe eczema should be made aware of eczema herpeticum and advised to seek help early. Children with atopic eczema, especially those with a history of eczema herpeticum, should avoid close contact with relatives and friends with active herpes simplex.

Secondary bacterial infection with *S aureus* or ß-haemolytic streptococci may occur which may be indicated by yellow crusting. The secondary infection may be heralded by a high fever and other systemic symptoms. A more severe complication is periorbital eczema herpeticum that can result in keratoconjunctivitis with possible stromal scarring and subsequent blindness. Patients who have eye involvement require immediate ophthalmologic evaluation.

Treatment: Severe cases require acyclovir, as early as possible for 7 days and oral antibiotics if secondary bacterial infection is suspected. The underlying eczema should be treated to avoid recurrences. EH is not necessarily more common in HIV, but needs higher and longer doses of treatment.

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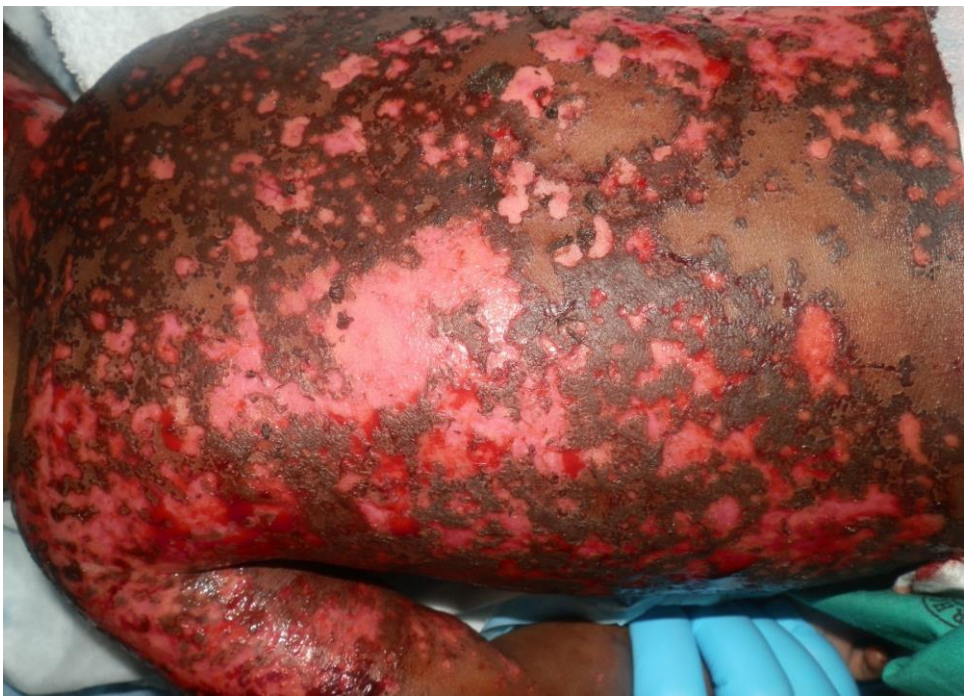

Figure 19: Eczema herpeticum. Shallow and punched out ulcers, widespread on trunk and face. Some ulcers have coalesced to form large haemorrhagic ulcers.

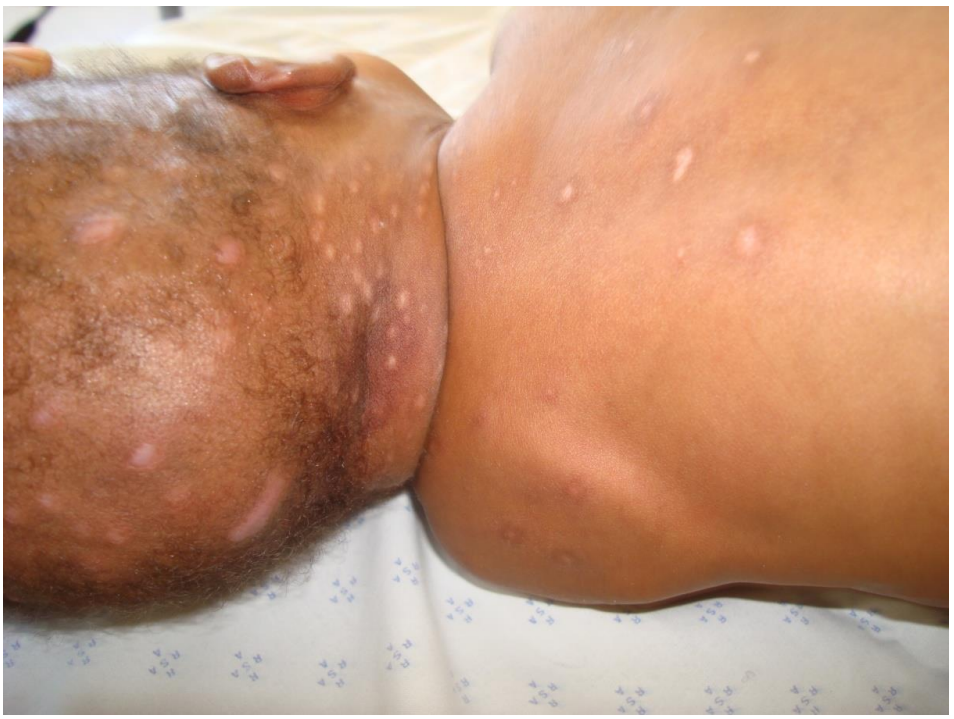

Figure 20: Eczema Herpeticum: Residual lesions in a 4 month old child treated 4 weeks earlier for eczema herpeticum.

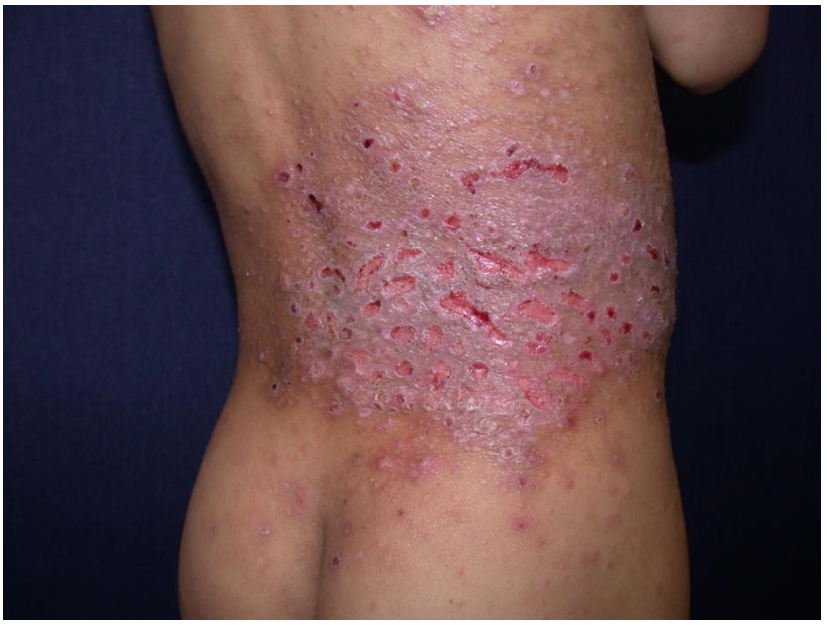

Figure 21: Punched out ulcers of eczema herpeticum confined to plaques of eczema in a child with atopic dermatitis.

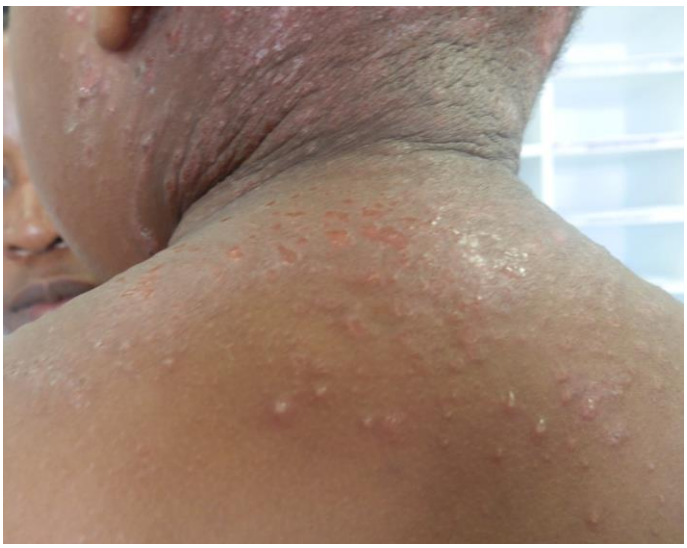

Figure 22: Eczema herpeticum. A combination of vesicles and shallow, punched out ulcers in the background of atopic eczema. Differential diagnosis to consider: Acute contact dermatitis.

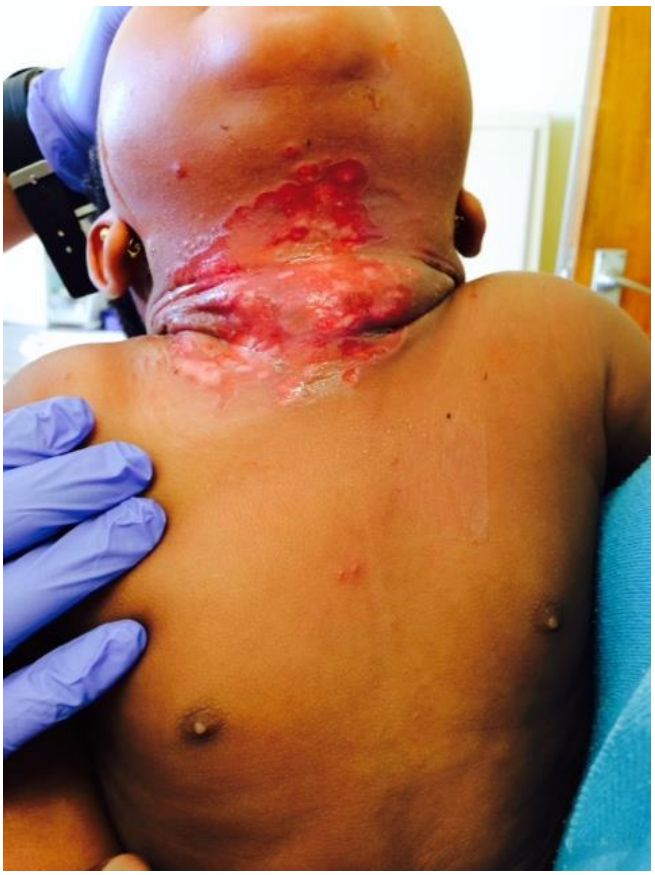

Figure 23: Severe confluent ulcers of eczema herpeticum on the neck of a child with atopic dermatitis

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Herpes Zoster (Shingles)

Herpes zoster is rare in immunocompetent children but an increased incidence is described in HIV-infected persons, sometimes as an early clinical sign of the development of AIDS.

Description: It is usually localized to a dermatome as a result of reactivation of the dormant virus in the sensory ganglion acquired during primary varicella or chicken pox infection. The word zoster means a girdle because it passes round the body like a girdle.

Aetiology: Is caused by a neurodermotropic virus called varicella zoster virus. It follows a clinical or sub clinical varicella (chicken pox) infection early in life or occasionally in utero. Predisposing factors include HIV infection, chronic steroid use, malignancies and diabetes mellitus.

Clinical presentation: The prodromal symptoms are hyperesthesia, paresthesias, burning dysesthesias or pruritus along the affected dermatome(s). The most common presenting features are pain and vesiculations Thoracic and cranial nerves are the most commonly involved. In most situations herpes zoster is confined to a single dermatome but can be multidermatomal or disseminated in HIV-infected children.

Epidemiology: It is distributed worldwide and is a common complication of HIV.

Diagnosis: Diagnosis is mainly clinical but in cases of uncertainty, Tzanck smear, viral culture, PCR is helpful.

Prevention: Varicella zoster vaccine in susceptible individuals.

Treatment: Rest and analgesics are sufficient for mild attacks of zoster in the young. Soothing antiseptic applications may be helpful and secondary bacterial infections require antibiotics. Treatment of HZ is with antivirals: acyclovir 200mg five times a day for 7 days or IV acyclovir 5 mg/kg 8-hourly. In case of acyclovir resistance: Where available: Famciclovir and valacyclovir are other options. Foscarnet 120-200 mg in two to three divided doses, in case of acyclovir resistance or when available. The antiviral medications are most effective when started within 72 hours of onset of the rash. Opioids, tricyclic anti-depressants and anti-convulsants are useful in managing post-herpetic neuralgia.

Complications: Post-herpetic neuralgia, secondary bacterial infections. Recently, a vaccine has been developed for varicella zoster, which should reduce the population frequency of post-herpetic neuralgia. Encephalitis other main systemic complications are varicella pneumonia and hepatitis.

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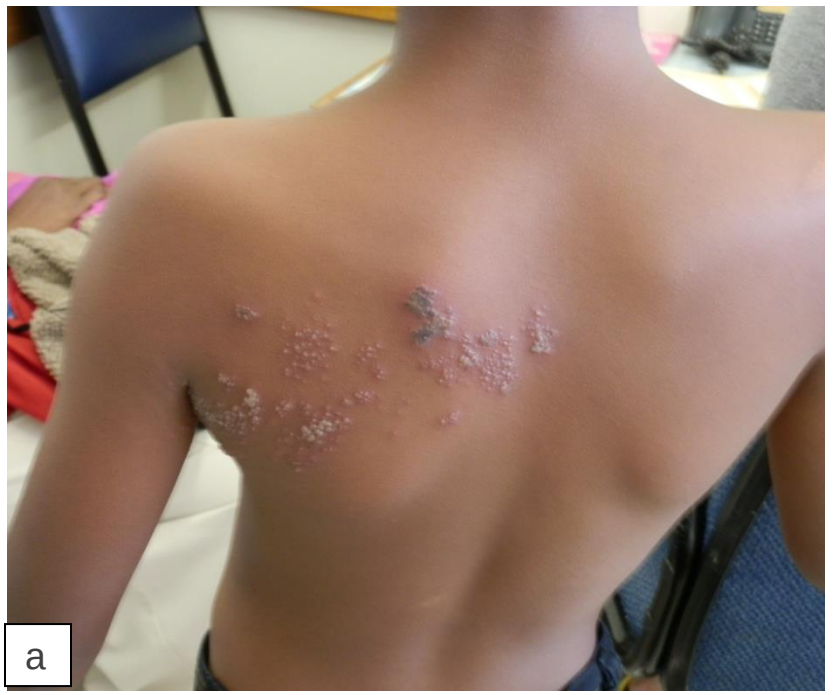

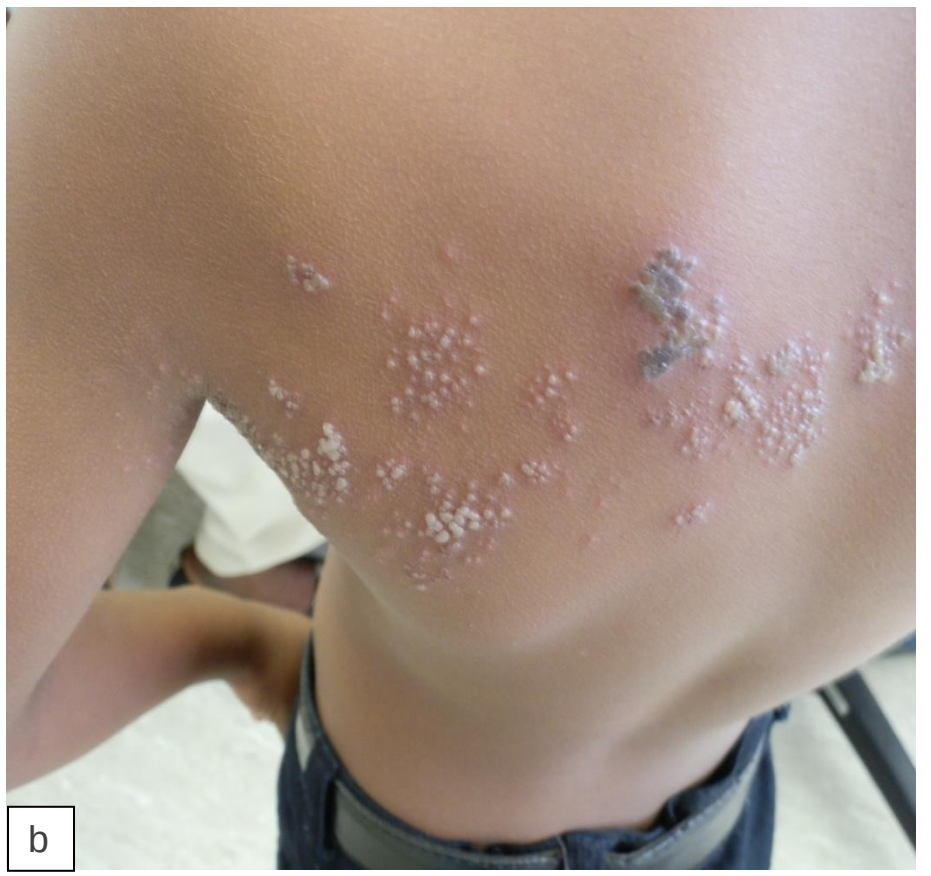

Figure 24a and b: Herpes zoster showing: grouped vesicles and pustules lesions with some crusting in T1/T2 dermatomal distribution.

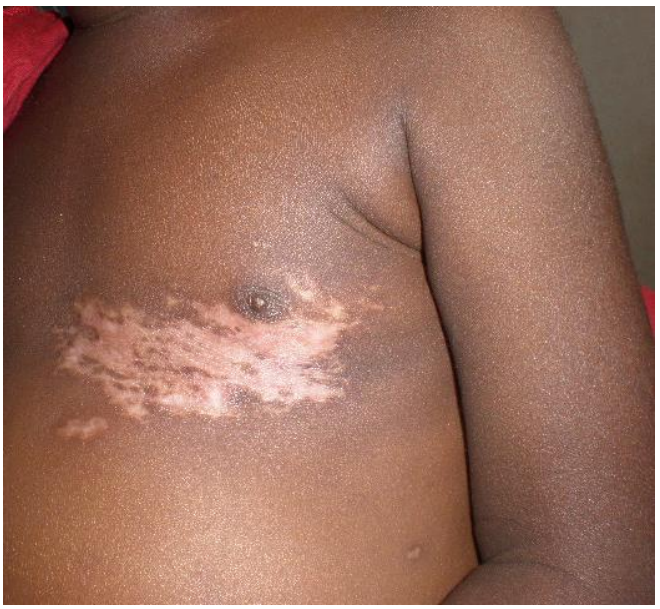

Figure 25: Healed Herpes zoster showing scarring and post-inflammatory hypopigmentation.

Viral Warts

The different morphological variants of warts are found in 5-30% of patients with HIV infection.

Plane Warts (Verruca Plana)

Description: These are flat warts (verruca plana)

Aetiology: Human papilloma virus (HPV) type 3 and, less often, types 10, 27, and 41 are the causative agents of verruca plana.

Clinical presentation: The warts are very slightly elevated above the level of surrounding skin and can be slightly hypo or hyperpigmented. Plane warts in HIV infection tend to be extensive and may be photodistributed.

Epidemiology: Plane warts are common and have no gender predilection. Prevalence of about 20% in HIV-infected children has been reported. Transmission can be either directly through person to person contact or indirectly through sharing of fomites.

Diagnosis: Diagnosis is mainly clinical. In cases of doubt PCR and histology are helpful.

Prevention: Healthy skin care and avoiding skin contact with an infected person.

Treatment: Response to treatment is usually unsatisfactory. Treatment options include salicylic or lactic acid in flexible colloidal preparations and 0.05% tretinoin creams. Initiation of ART does not seem to improve plane warts.

Complications: Potential risk of development of HPV associated epithelial neoplasia.

Further reading

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6. Anonymous. Clinicians should check women with HPV for HIV. Aids Alert 1999; 14: 39–41.

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Epidermodysplasia verruciformis

Description: Epidermodysplasia verruciformis (EV) is an inherited clinical variant of verruca plana in which there is widespread and persistent infection with HPV. Patients frequently harbor multiple HPV subtypes. Subtypes 5 and 8 are associated with squamous cell carcinomas. The other subtypes are 14, 17, 20 and 47.

Clinical presentation: A characteristic combination of plane warts, pityriasis versicolor-like lesions and reddish plaques.

Complication: Malignant transformation occurs in 20 - 40% of patients and onset is usually in the 20s. However metastatic disease is rare.

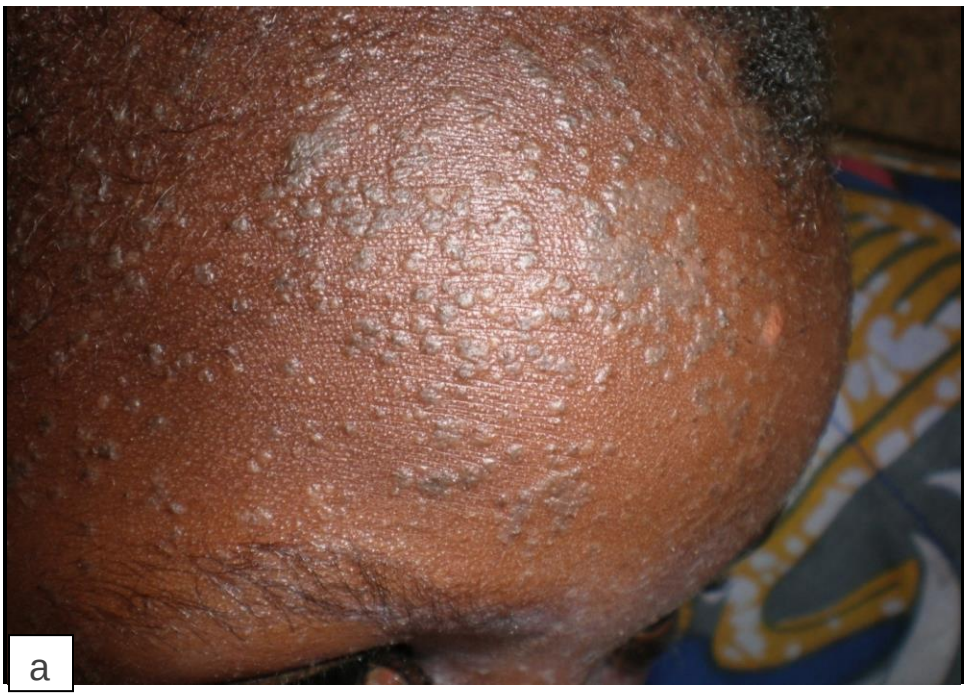
Prevention: Avoidance of excessive sun exposure, with diligent use of effective sunscreen.

Treatment: Patients should be observed for the development of squamous cell carcinomas and premalignant lesions, which should be excised or locally ablated. Oral retinoids have been used but their long-term effectiveness is uncertain.

First-line option: etretinate, starting dose of 1 mg/kg/day, but the effect is dose dependent and relapse occurs if the drug is stopped.

Second-line option: The combination of etretinate plus IFN-α may also produce a useful clinical effect.

Other options include oral isotretinoin, which has been shown to improve the clinical appearance of the benign lesions. Occasional but inconsistent benefits have been reported with topical imiquimod, topical vitamin D analogues, topical immunotherapy with squaric acid dibutylester and oral cimetidine.



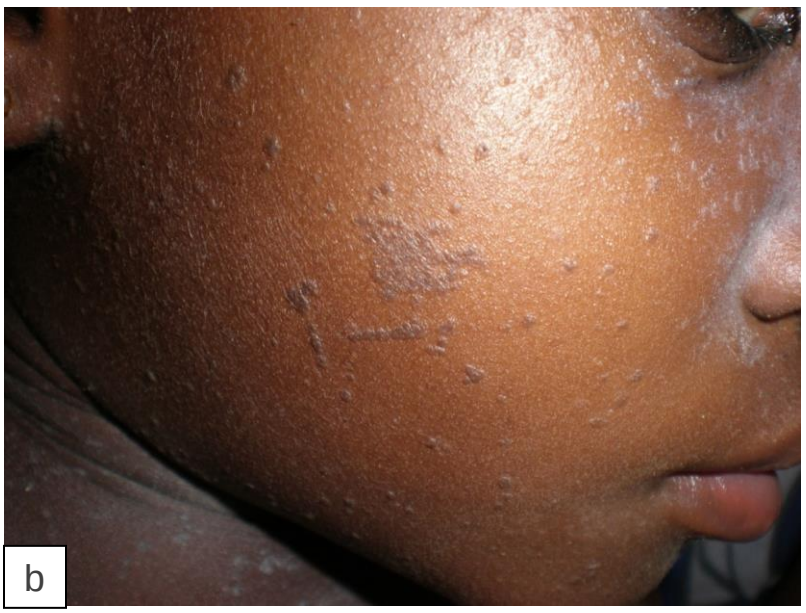


Figure 26a and b: Hyperpigmented flat warts on the face of a child. Note the linear arrangement on the cheek following lines of trauma, a phenomenon called koebnerization or isomorphic response.

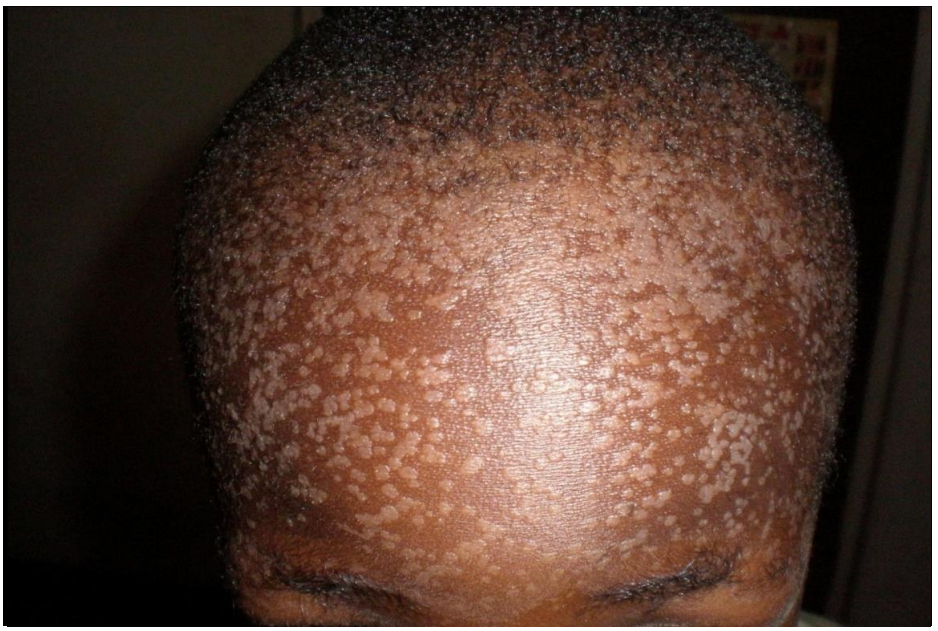


Figure 27: Flat hypopigmented plagues on the forehead of a child with epidermodysplasia verruciformis. The lesion was initially misdiagnosed as tinea versicolor.

Palmoplantar and common warts

Clinical Presentation: Verrucous papules on palms and soles. Common warts can be verrucous, mosaic or filiform. Periungual involvement common.

Epidemiology: HIV-infected children are more susceptible and the warts tend to be more extensive and recalcitrant.

Diagnosis: The diagnosis is based upon clinical appearance. Paring of overlying hyperkeratotic debris usually reveals thrombosed capillaries. This helps to differentiate warts from calluses. In cases of doubt PCR and histology are helpful.

Prevention: Advice on simple measures to limit the spread of the infection by avoiding physical contact with the warts and cleaning of fomites may be advised.

Treatment: Treatment options include salicylic acid, cantharidin, topical 5-fluorouracil, cryotherapy, paring, cautery or CO_2 laser.

Further reading

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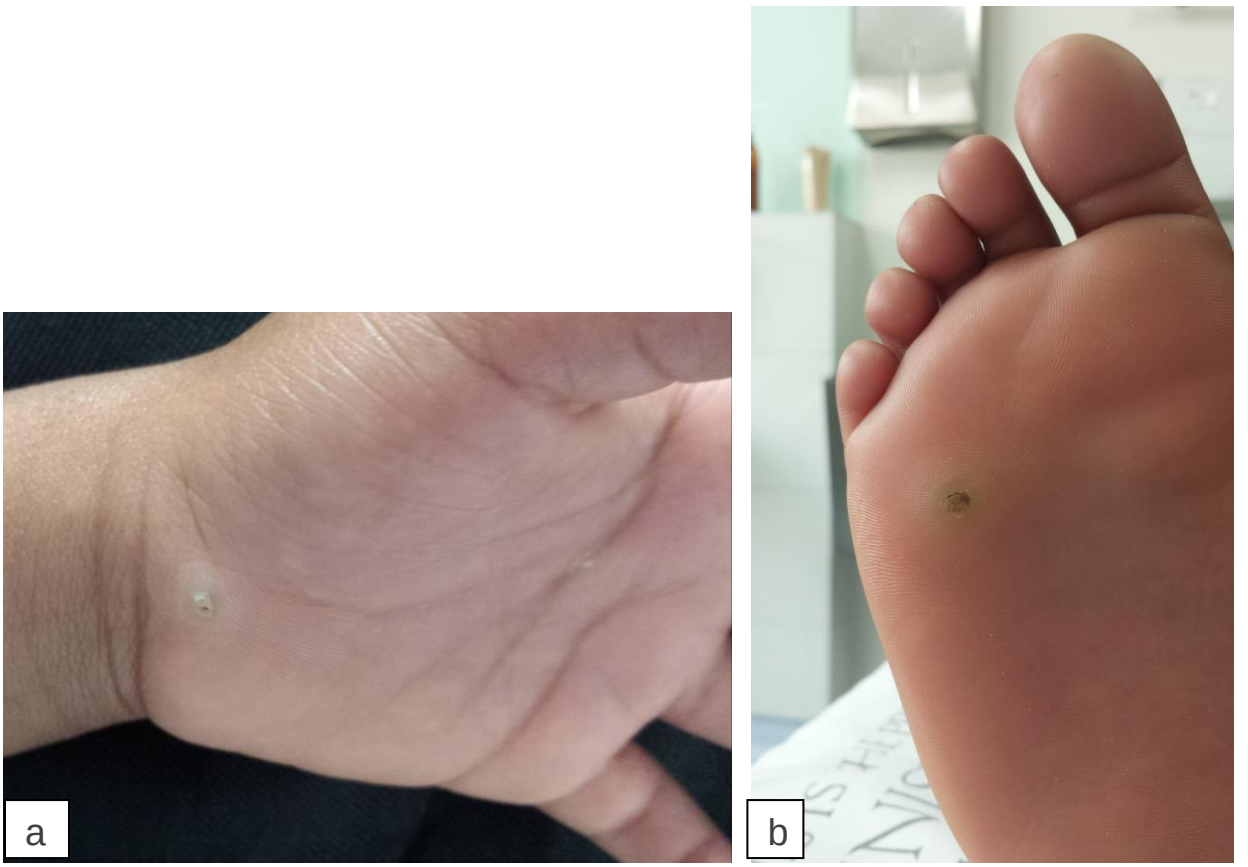

Figure 28a and b: Palmar and plantar warts on the sole and palm of a child.

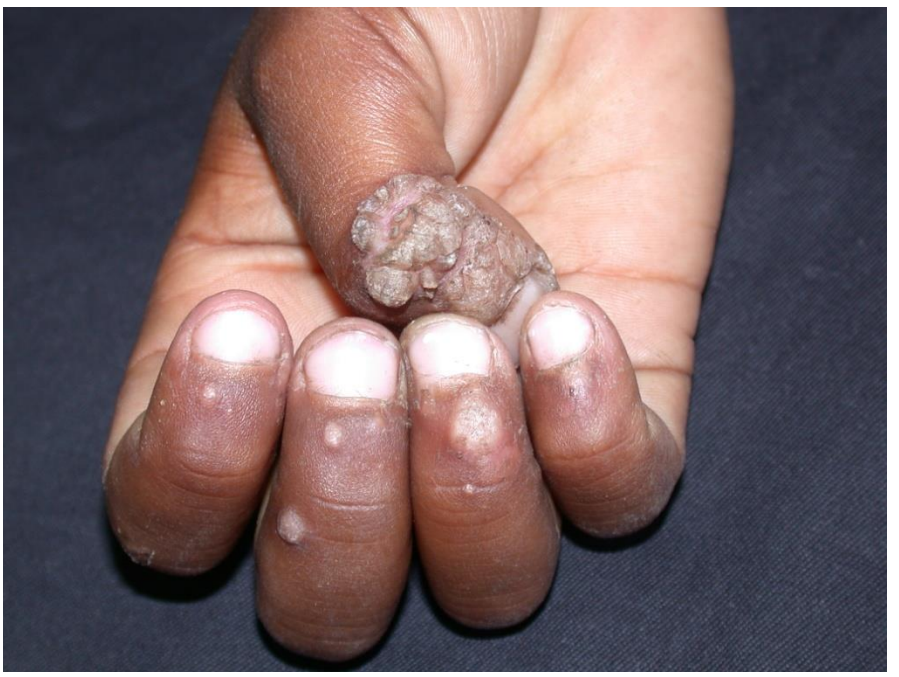

Figure 29: Common warts presenting as multiple papules on distal end of fingers, together with a much larger hyperkeratotic, verrucous plaque on the distal end of the left thumb.

Oral warts (Heck's Disease)

Clinical Presentation: Whitish or pale papules with a smooth or roughened surface. Can affect any part of the oral cavity.

Epidemiology: HIV-infected children are more susceptible to oral warts, which are rare in immunocompetent persons. In the era of ART, the prevalence of oral warts is increasing estimated to be between 1.6 – 2.6%.

Diagnosis: Diagnosis is mainly clinical. In cases of doubt PCR and histology are helpful. Human papilloma virus types 13 and 32 are the most commonly implicated.

Prevention: Avoid biting warts in other areas of the body.

Treatment: Treatment options include surgery, cautery or CO_2 laser. Topical imiquimod 5% cream has been successfully used.

Complications: Potential risk of development of HPV associated epithelial neoplasia.

Further reading

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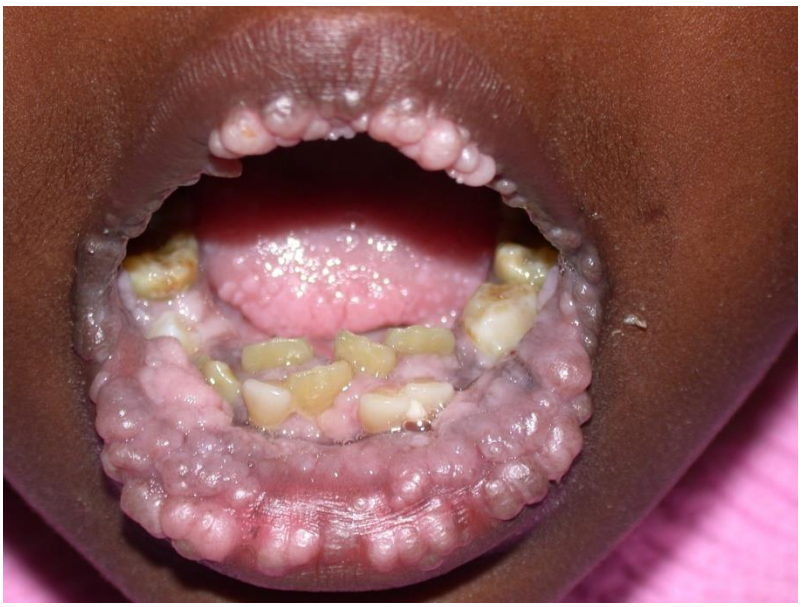

Figure 30: Warts - longstanding oral lesions in an HIV-infected child affecting alignment of teeth.

Genital Warts and Perianal Warts

Description: Warts on the genital and perianal area have variable clinical presentations.

Aetiology: At least 40 subtypes of human papilloma virus (HPV) have been shown to cause genital warts. Of these subtypes 16 and 18 are considered to be high risk as they are associated with development of squamous cell carcinomas,

Clinical presentation: anogenital warts (condylomata acuminata) may present as flat, dome-shaped, cauliflower-shaped, or pedunculated lesions.

Epidemiology: Anogenital warts are common sexually transmitted disease estimated to occur in 1% of sexually active adults. In young children, they may be an indication of sexual abuse.

Diagnosis: Diagnosis of anogenital warts is mainly clinical and the diagnosis can be confirmed by histology or PCR. The latter is used for subtyping to rule out high risk subtypes.

Prevention: Advice on simple measures to limit the spread of the infection by avoiding physical contact with the warts and cleaning of fomites may be advised. HPV vaccines are effective for prevention of HPV-associated malignancies.

Treatment: Not all warts need treatment as many give little inconvenience and will resolve spontaneously. Where treatment is needed first-line options include 20% podophyllin, cryotherapy and salicylic acid. Second-line options include imiquimod. Spontaneous remission has been reported in 20-30 of infected patients.

Complications: Potential risk of developing HPV associated epithelial neoplasia exists. Genital warts in children may be a manifestation of child abuse.

Further reading

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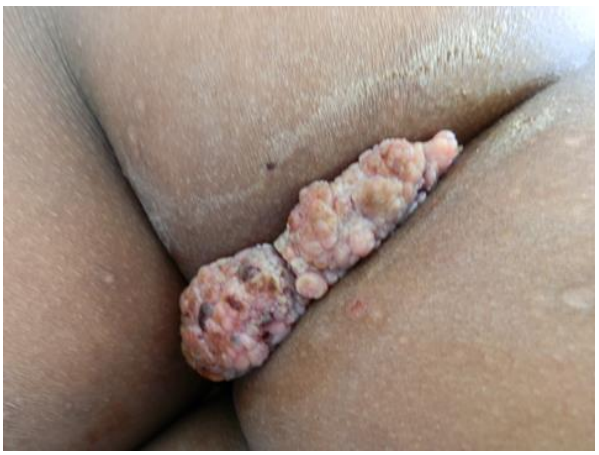

Figure 31: Perineal warts

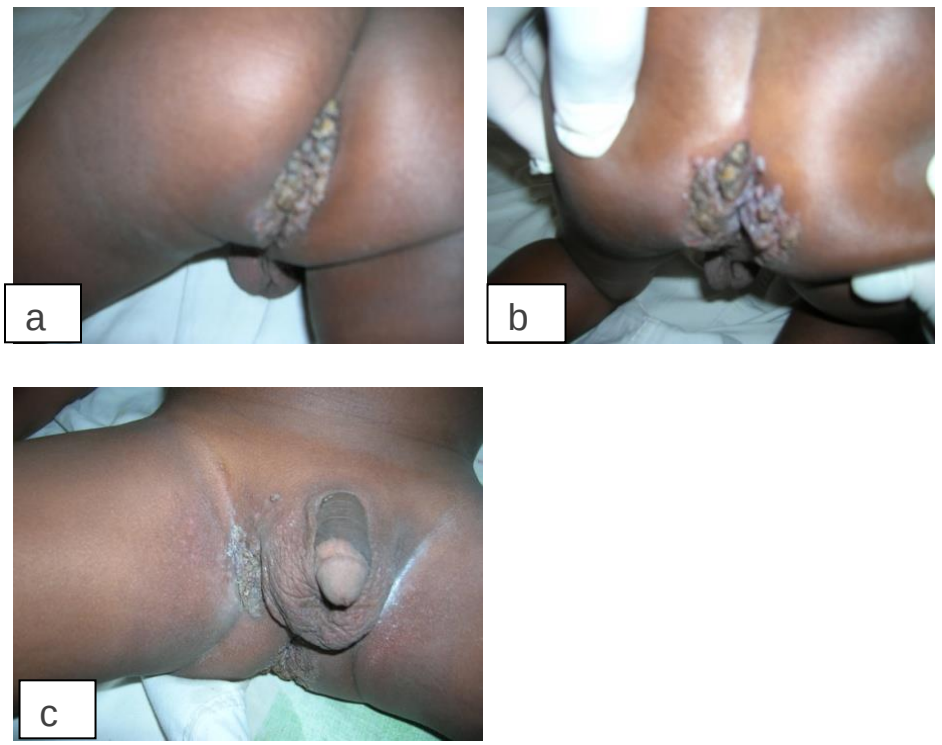

Figure 32a, b and c: Perianal and perineal warts in a 2-year-old boy. The mother also had perineal warts.

Measles (Rubeola)

Description: A contagious disease caused by measles virus with characteristic rash that starts from the face and spreads to the extremities.

Aetiology: Measles is caused by the measles virus. Lack of immunization is a risk factor although disease has been recorded among immunized infants. Vitamin A deficiency state has been associated with severe disease.

Clinical presentation: High grade fever is usually the first sign of measles at about 10 to 12 days after exposure to the virus, and lasts four to seven days. Other symptoms in the initial stage are catarrh, cough, red and watery eyes, and small white spots inside the cheeks (Koplik's spots). Koplik's spots are pathognomonic for measles but last for less than 24 hours. A maculopapular rash follows, usually on the face and upper neck after several days and then spreads to reach the hands and feet. The rash lasts for five to six days, and then fades. On average, the rash occurs 14 days after exposure to the virus (range 7 – 18 days).

Epidemiology: The incidence in Africa is estimated to be as high as 17. 2 cases per 100,000 population. There is a higher incidence of contracting measles in HIV-infected children. In addition, there is an increased case fatality. Outbreaks of the disease still occur in parts of Africa. The virus is spread by close contact with infected nasal or throat secretions.

Diagnosis: Detailed history, including immunization history and a thorough physical examination for characteristic features should be done. Demonstration of measles IgM antibodies (where available) confirms the diagnosis.

Prevention: Routine measles vaccination for children (at 9 months of age) combined with mass immunization campaigns in countries with high case and death rates. The World Health Organization recommends two vaccinations at 6 and 9 months for HIV exposed and infected children. The vaccine is safe, effective and inexpensive. It may be given in combination with rubella and/or mumps vaccines in countries where these illnesses are problems. It is equally effective in the single or combined form.

Treatment: There is no effective anti-viral treatment. Supportive care is the mainstay and should ensure good nutrition, adequate fluid intake and treatment of dehydration. Antibiotics should be prescribed to treat secondary pneumonia and bacterial infections of the eye and ear. Two doses of vitamin A supplements, given 24 hours apart is recommended for all children diagnosed with measles in developing countries. Vitamin A supplements have been shown to reduce the number of deaths from measles by 50%.

Complications: Blindness, encephalitis, diarrhoea, otitis media, lower respiratory infections such as pneumonia

Further reading

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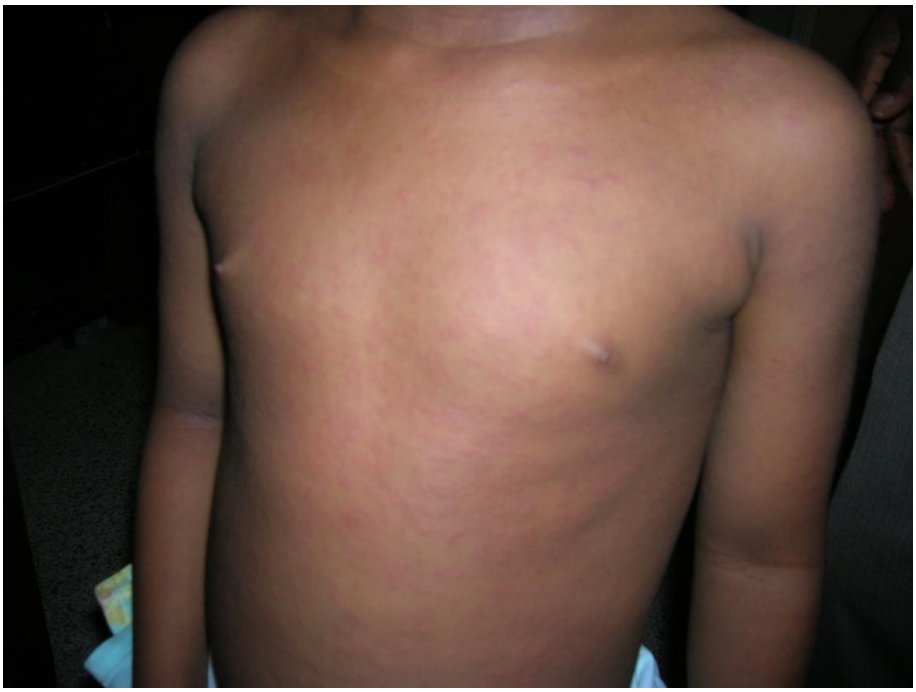

Figure 33: Measles: fresh maculopapular lesions.

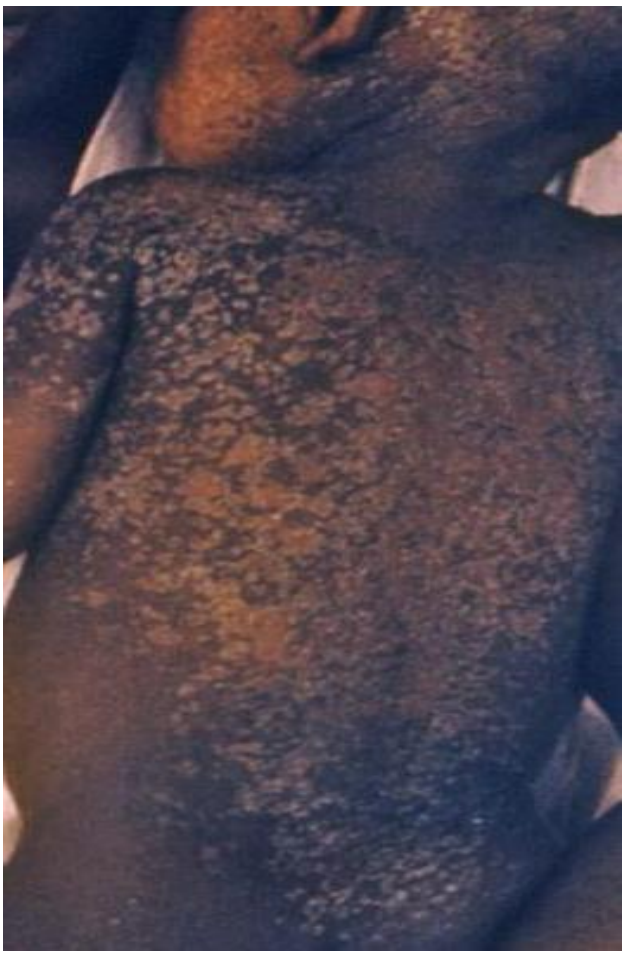

Figure 34: Measles: desquamating rash

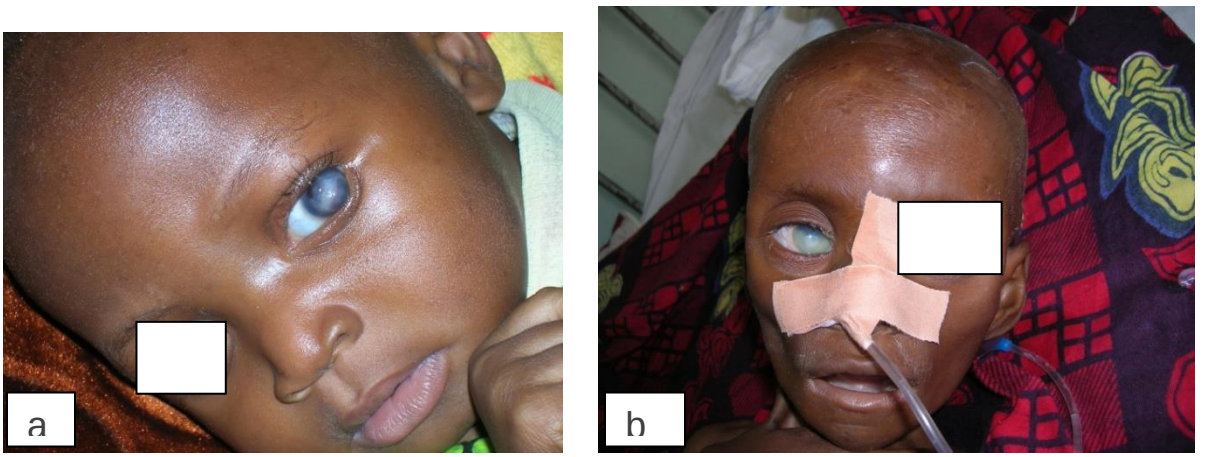

Figure 35a and b: Measles complication in two children: a. keratitis b. panophthalmitis

Molluscum Contagiosum

Description: Molluscum contagiosum (MC) is a common viral skin infection of the skin.

Aetiology: MC is caused by poxvirus – a DNA virus from the Poxviridae family.

Clinical presentation: Usually present as small pearly, dome shaped, small, discrete lesions with central umbilication. In HIV-infected individuals, atypical varieties such as large or non-umbilicated lesions are found. Individual papules may coalesce to form the agminate variety. Lesions tend to be recalcitrant and resistant to treatment.

Epidemiology: MC is seen in 10-20% of AIDS patients. Transmission is by autoinoculation and physical contact.

Diagnosis: mainly a clinical diagnosis but a skin biopsy staining of the curdy material with Giemsa and demonstration of eosinophilic molluscum bodies can be helpful in atypical cases.

Prevention: Avoidance of close contact with infected persons.

Treatment: Infection is usually self-limiting and spontaneously resolves after 18-24 months in mild cases and therefore no treatment may be necessary. If problematic and extensive the most commonly used therapeutic options include 5% salicylic acid/lactic acid preparations, trichloroacetic acid, curettage, cautery and cryotherapy. Less commonly imiquimod cream, tretinoin cream, cantharidin and benzyl peroxide are used with variable success. Large lesions can be removed surgically. Treatments may cause scarring and leave marks long term. HAART improves outcome in HIV-infected children and should be considered in eligible patients.

Complications: Infected and inflamed MC can cause disfigurement and scarring.

Further reading

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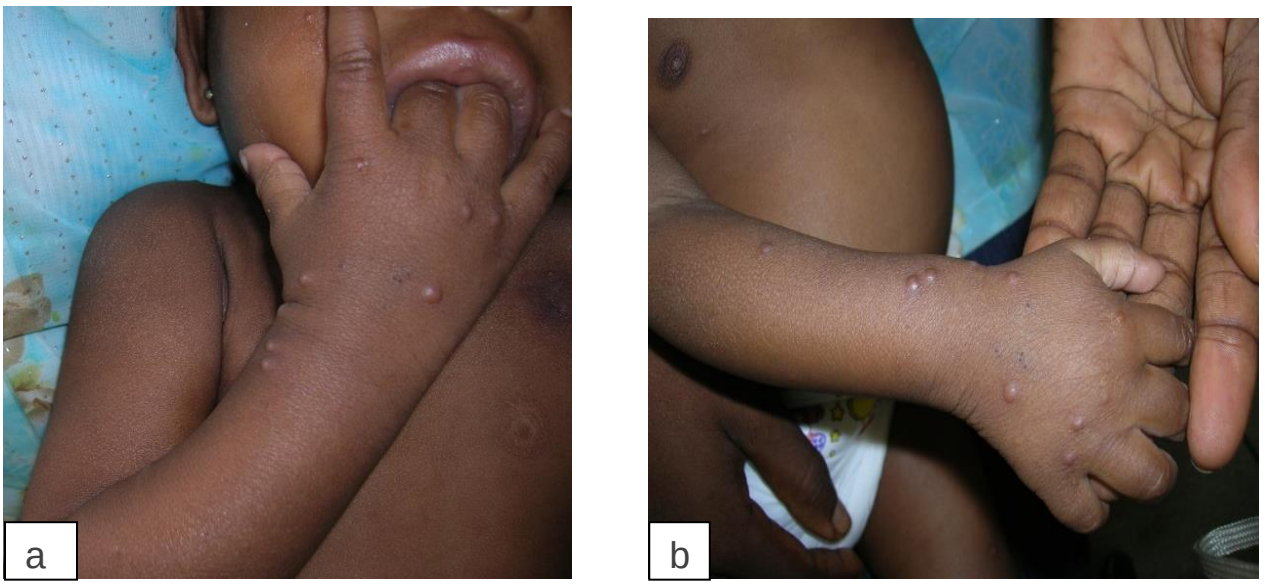

Figure 36a and b: Molluscum contagiosum in HIV- 12 month old girl, the lesion involved the extremities and the face (not shown). A differential diagnosis is papular urticaria.

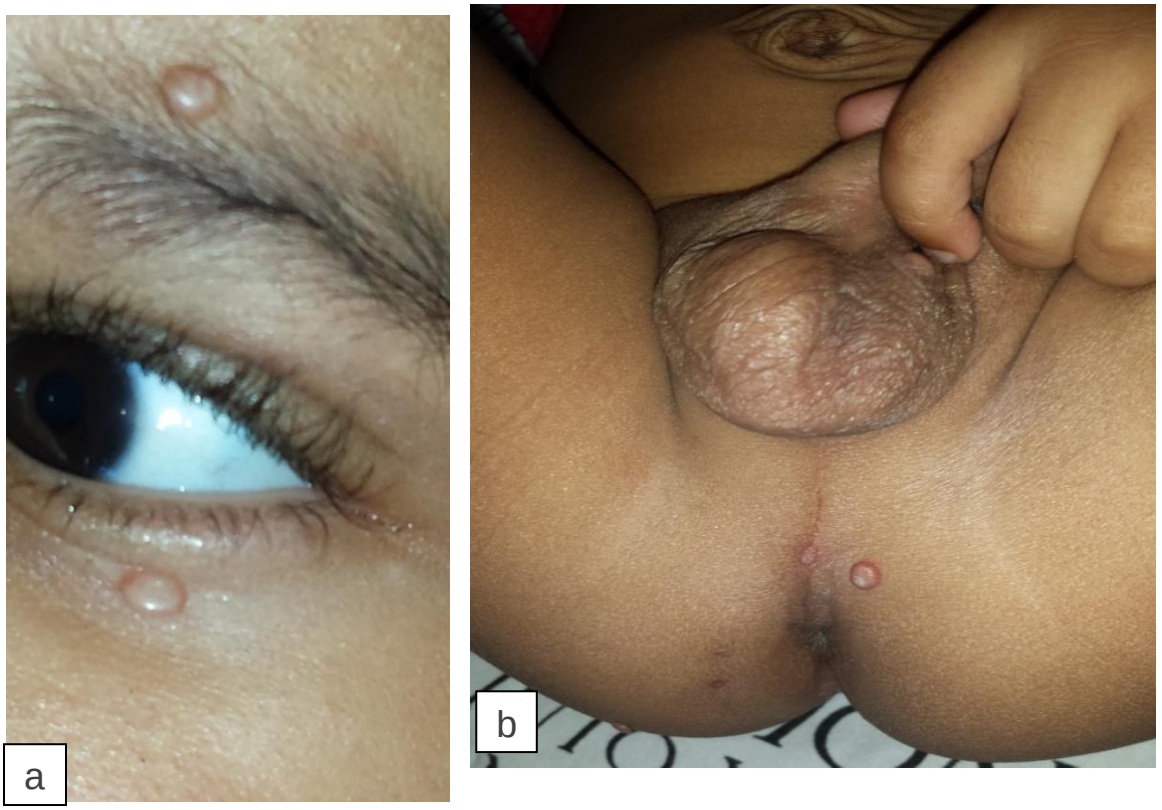

Figure 37a and b: Molluscum contagiosum appearing below the eyelid and peri-anal regions 3 months after commencing ART in an 8-month-old child.

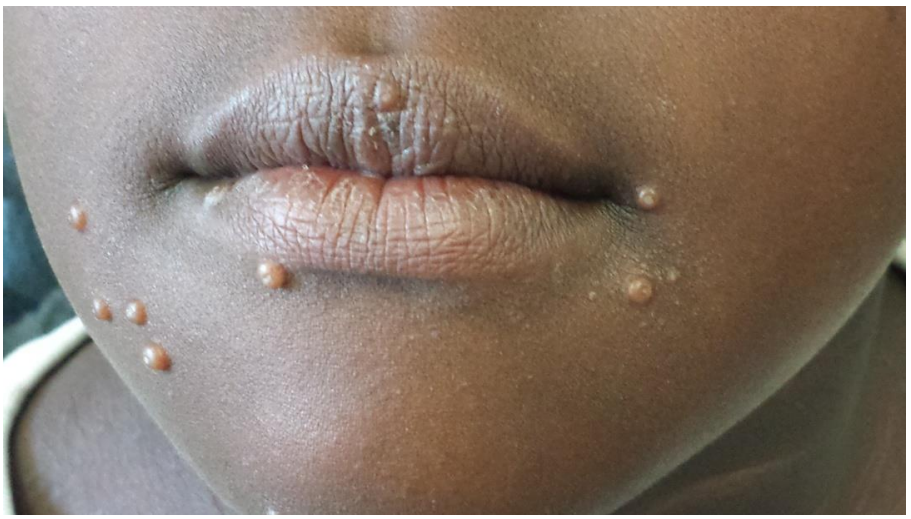

Figure 38: Multiple mollusca in the perilabial region in a 6-year-old girl several years after antiretroviral therapy was started and she had achieved complete viral suppression.

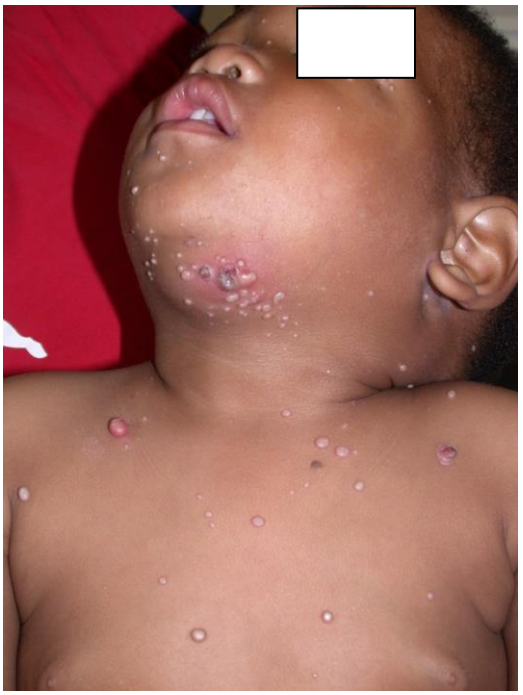

Figure 39: Multiple molluscum lesions on the face, neck and upper chest in an HIV-infected child. Lesions are of different sizes and are at different stages of evolution. Secondary infection and inflammation are common.

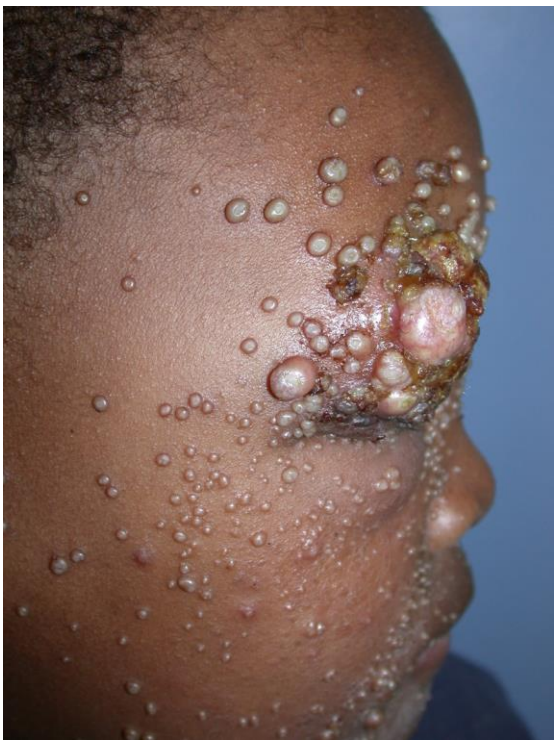

Figure 40: Extensive molluscum in an HIV-infected child on the face involving the eyelid. Note the giant molluscum.

Table 2: Treatment options: Viral infections

Infection	First-line treatment	Alternative treatment	Where available
HSV	Acyclovir	Valacyclovir Famciclovir	Foscarnet
Eczema Herpeticum	Acyclovir	Valacyclovir Famciclovir	Foscarnet
Herpes Zoster	Acyclovir	Valacyclovir Famciclovir	Foscarnet
Verruca Plana	Salicylic/lactic acid	0.05% tretinoin creams	
EDV	Oral cimetidine	Isotretinoin etretinate plus IFN-α	-Imiquimod -Vitamin D analogue -Squaric acid dibutylester
Genital Warts	20% Podophyllin	Imiquimod	
Molluscum contagiosum	5% salicylic Acid/lactic acid benzoyl benzoate	-Trichloroacetic acid -Liquid nitrogen -Tretinoin cream	Curettage Cautery Imiquimod cream Cantharadin
Measles	Vitamin A supplements	Antibiotics as required	

EDV- Epidermodysplasia verruciformis

CHAPTER 3: FUNGAL SKIN INFECTIONS

Superficial Fungal Infection

Dermatophytosis

Description: Dermatophyte infections are common in HIV-infected children. They include: tinea capitis, tinea corporis, tinea unguium and tinea pedis.

Tinea

Aetiology: These infections are caused by fungi called dermatophytes, which produce an enzyme called keratinase to break down keratin.

Clinical presentation: Depends on part of the body affected. In the skin, it presents as "rings" (ring worm), with raised edges and clearing at the centre of the lesions, alopecia in the scalp (tinea capitis), may present with scaly feet and/or macerated web spaces (tinea pedis) or may involve the nails leading to the destruction and discoloration of the nails (tinea unguium).

Epidemiology: Common around the world. Specific fungal aetiology varies from one geographical region to another.

Diagnosis: Is mainly clinical but a simple potassium hydroxide (KOH) preparation may be helpful. A KOH mount can be easily prepared by gently scraping the infected skin or blister roof with a sterile scalpel blade onto a glass slide with 1 to 2 drops of 10% KOH. The sample is then examined under the microscope for the presence of hyphae. Alternatively, specimen can be sent for fungal culture for identification of the causative organism and Under Wood's lamp (UV) colonies will fluoresce.

Prevention: Changing footwear frequently, drying feet well after bathing (especially between toes), refraining from sharing articles of clothing, and appropriately treating friends and family members of affected patients, can be very helpful in minimizing risks of exposure and reinfection.

Treatment: The treatment of dermatophyte infections usually involves the use of oral terbinafine, fluconazole, itraconazole, griseofulvin or one of several well-tried topical preparations.

A commonly used oral antifungal of choice is griseofulvin 10-20 mg/kg for at least 6 weeks for skin and hair infection, 6 weeks for tinea capitis and in severe hair, skin and scalp infections, up to 3 months.

Generally, topical therapies are used for localized or mild infections, oral antifungals for the more extensive infections. There is a variety of topical antifungal agents, including clotrimazole, econazole,

oxiconazole, miconazole, terbinafine, and naftifine applied to the affected areas twice daily for 2 to 4 weeks.

For nail infections, longer therapy with oral agents is usually necessary. However, children respond better to topical therapy than adults because of a thinner nail plate and potentially faster nail growth rate.

Complications: Secondary bacterial infection and ID reaction (autoeczematisation as a hypersensitivity reaction to the fungus).

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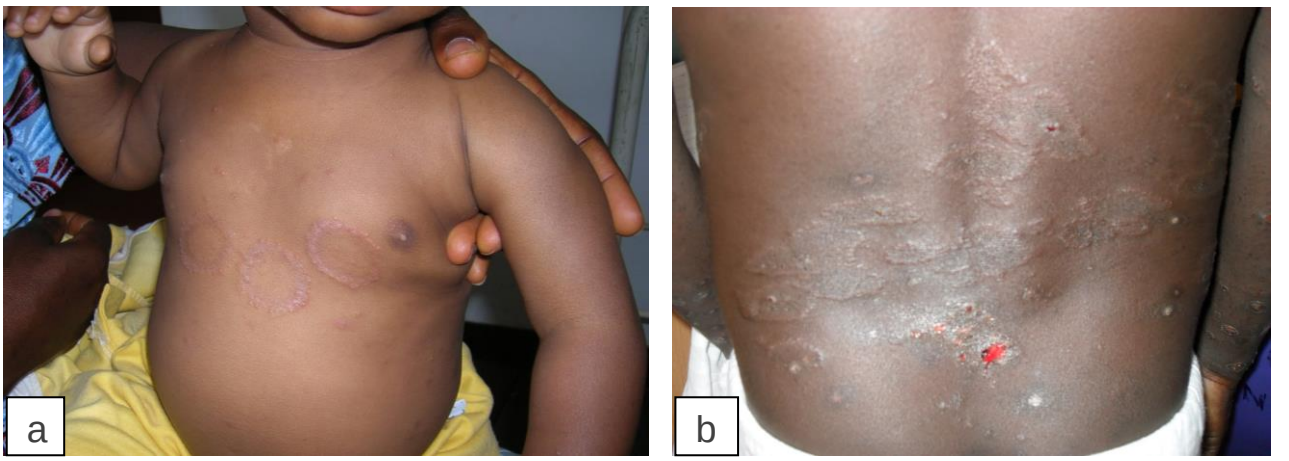

Figure 41a and b: Tinea corporis lesions on the trunk. Well demarcated lesions with raised edge and central clearing.

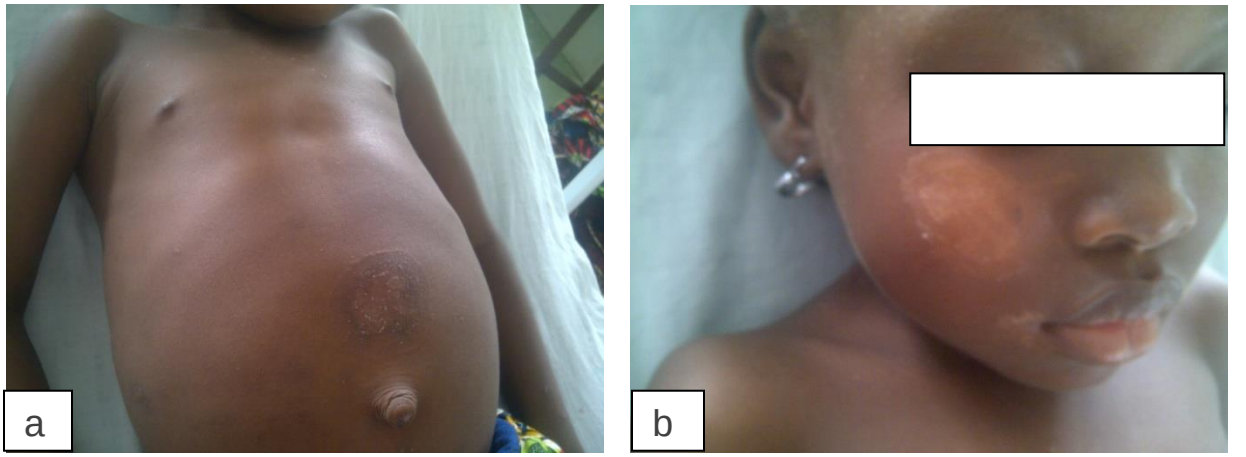

Figure 42 a and b: Tinea corporis on the anterior abdominal wall and right cheek. Note the ring shaped scaly lesion with central area of clearance.

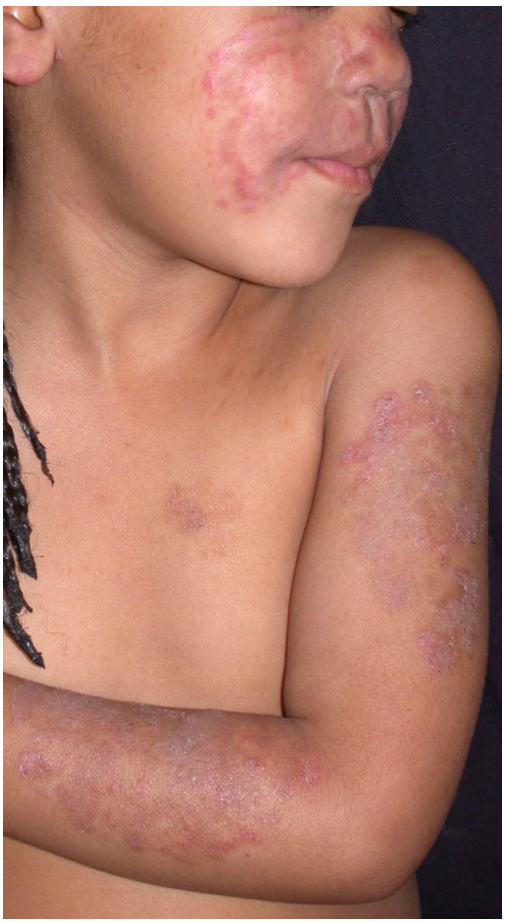

Figure 43: Annular plaques of tinea faciale and corporis on a child. Note multiple rings.

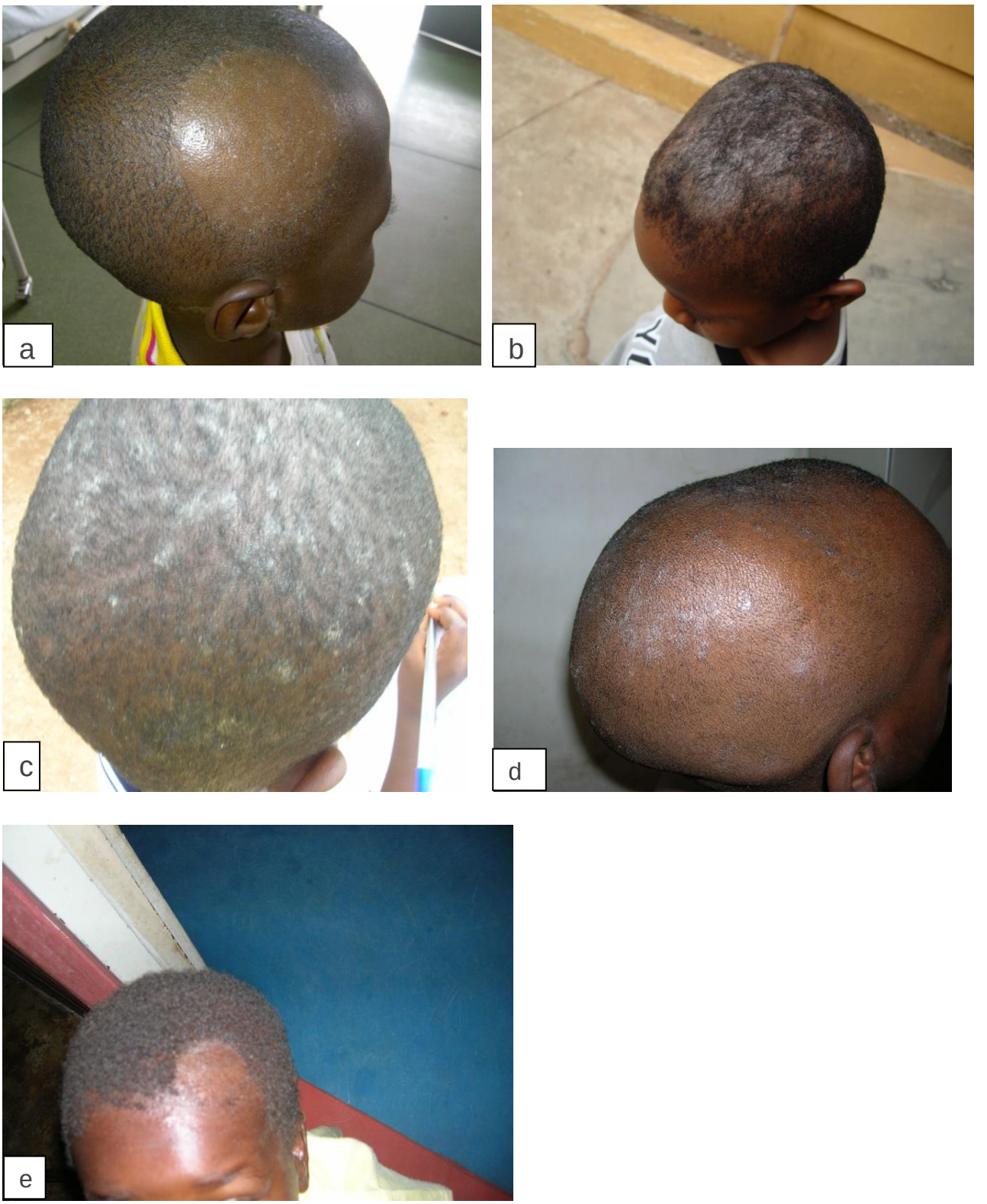

Figure 44 a, b, c, d and e: Variants of tinea capitis on the scalp of 5 children.

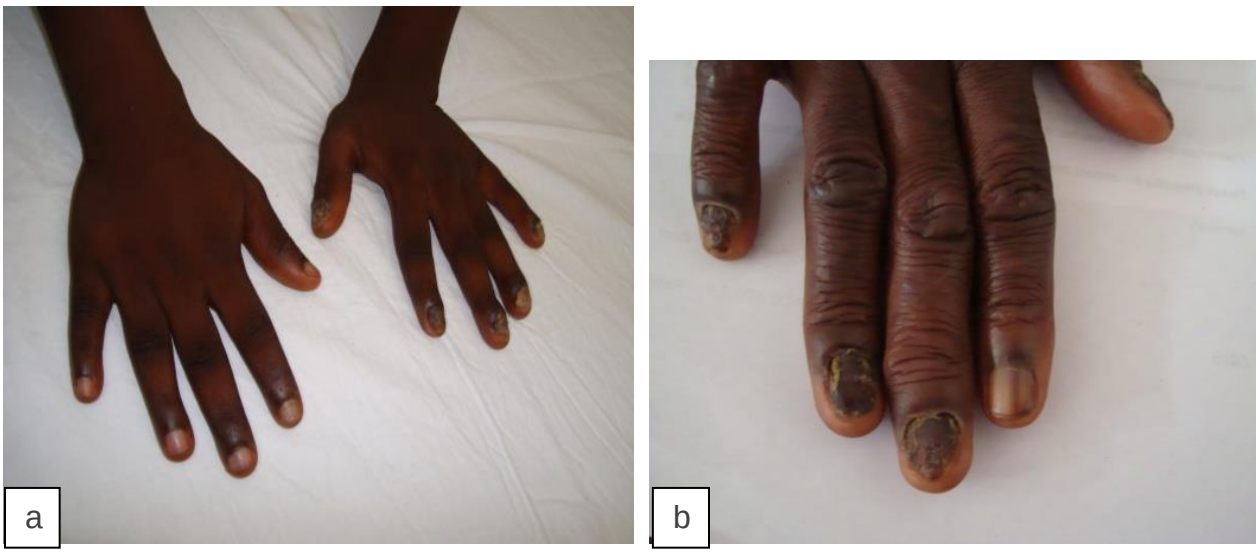

Figure 45 a and b: Tinea unguium in a 5-year-old boy (left) and in his mother (right); both presenting in the ART clinic.

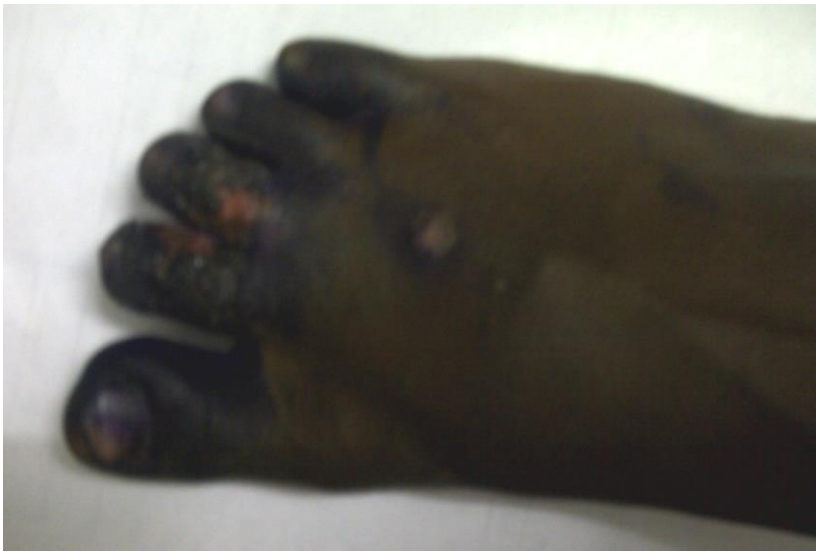

Figure 46: Tinea pedis. Gentian violet applied on the lesion.

Inflammatory Tinea

Tinea infections results in diverse clinical features, ranging from the carrier-state to severe tinea corporis with heavy inflammation.

Although the clinical features of tinea may be similar to those seen in adults with erythema and scaling, signs of dermatophyte infection in children may be nonspecific and mimic other conditions, such as psoriasis, atopic dermatitis, contact dermatitis, dyshidrotic eczema, juvenile plantar dermatosis, impetigo, herpetic infection, and cellulitis. Vesicles and bullae may also be more common in children with inflammatory tinea, mimicking bacterial or herpetic cellulitis.

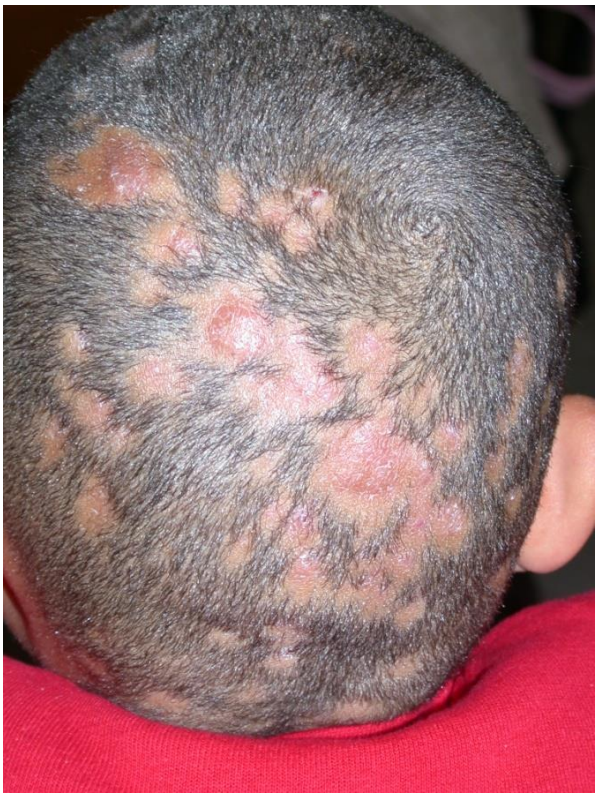

Figure 47: Inflammatory tinea capitis. Note the boggy masses associated with alopecia and scarring.

Pityriasis Versicolor (Tinea Versicolor)

Description: A mild, chronic infection of the skin caused by *Malassezia* yeast.

Aetiology: Is caused by the fungi *Malassezia* and the infection is milder and more superficial than the dermatophyte infections. Isolated species of *Malassezia* in patients include *M. globosa, M. sympodialis, M. furfur, M. obtusa,* and *M. restricta.*

Clinical presentation: The primary lesion is a sharply demarcated macule, sometimes slightly erythematous, but characterized essentially by fine, discrete or confluent branny scale that can be hyperpigmented or hypopigmented mainly on the upper trunk. The scale can be accentuated by stretching the lesions, making them scalier.

Epidemiology: Affects adolescents and adults. Prevalence of tinea versicolor is as high as 40% has been reported in the tropics. Climatic and local environmental factors account for variation in the prevalence seen in different geographical regions.

Diagnosis: This is mainly clinical but potassium hydroxide direct microscopy or visualization of the scaly lesions under Wood's lamp (UV), which shows the typical yellow fluorescence.

Differential diagnoses: Vitiligo and chloasma are normally distinguishable by their complete absence of scaling. Differential diagnoses include: seborrheic dermatitis, pityriasis rosea, secondary syphilis, pinta and tinea corporis.

Treatment: Selenium sulphide in a detergent base, available as shampoo or lotion in 1% or 2.5% concentrations (Selsun® shampoo Blue, Head & shoulders), applied to all the affected areas and left for 10 minutes before washing off or left overnight. In ordinary cases that settle spontaneously or as a result of treatment, the residual depigmentation may remain for many months without any scaling.

Other options include the topical azole antifungals (clotrimazole and ketoconazole). Terbinafine 1% cream is also effective. For widespread lesions topical ketoconazole, 2-3 applications may suffice.

For prophylaxis, selenium sulphide may be applied overnight once a month. Alternatives include 20% sodium hyposulphite solution, and 50:50 propylene glycol in water used long-term as suppressive therapy to prevent relapse.

Oral ketoconazole and itraconazole are also very effective especially when combined with topical antimycotics. Ketoconazole is not recommended in children <10 years. Fluconazole as a single 6 mg/kg dose may also be adequate but some patients may require longer periods of therapy. Itraconazole is active against pityriasis versicolor in a dose of 5 mg/kg usually given over 5 days.

Complications: In ordinary cases that settle spontaneously or as a result of treatment, the residual depigmentation may remain for many months without any scaling. Disfigurement of the affected areas and deep invasive infections may occur in untreated cases.

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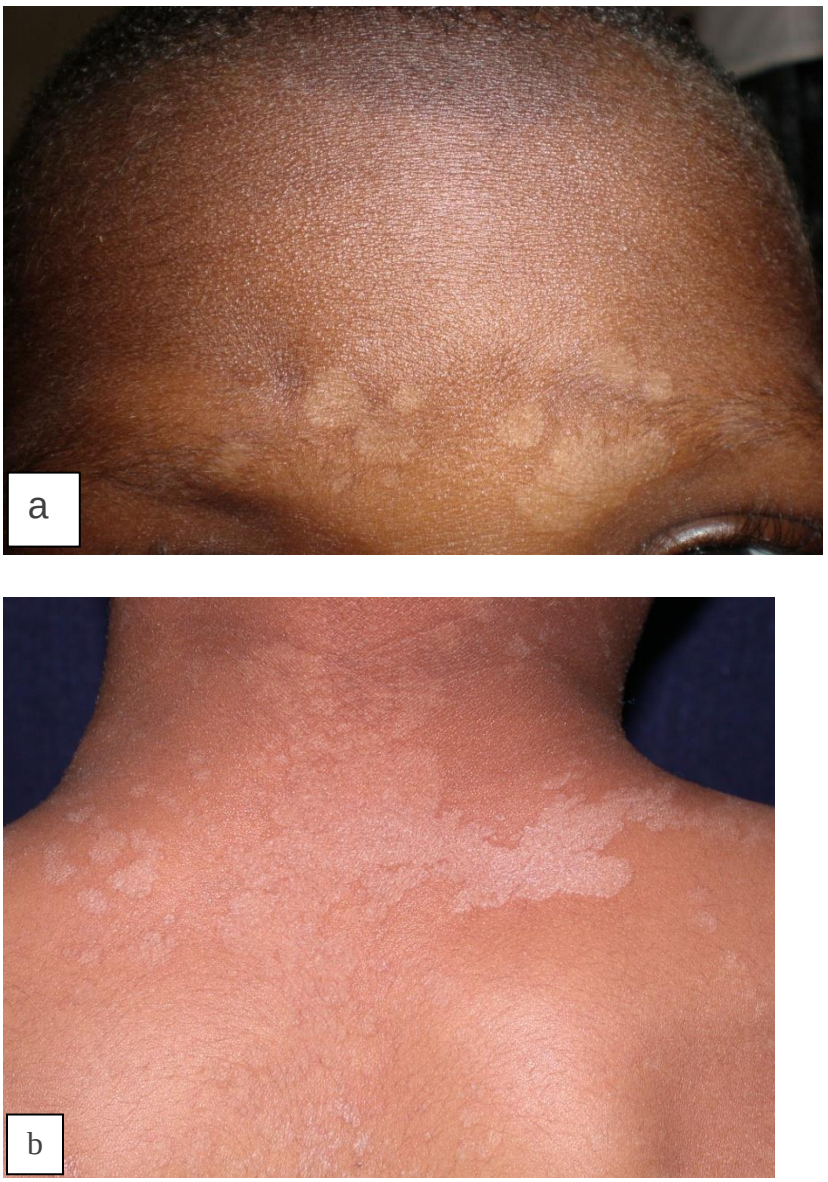

Figure 48a and b: Sharply demarcated macules with fine branny scaling on the forehead and back of children with tinea versicolor. Note the increased scaling after stretching the skin in (b).

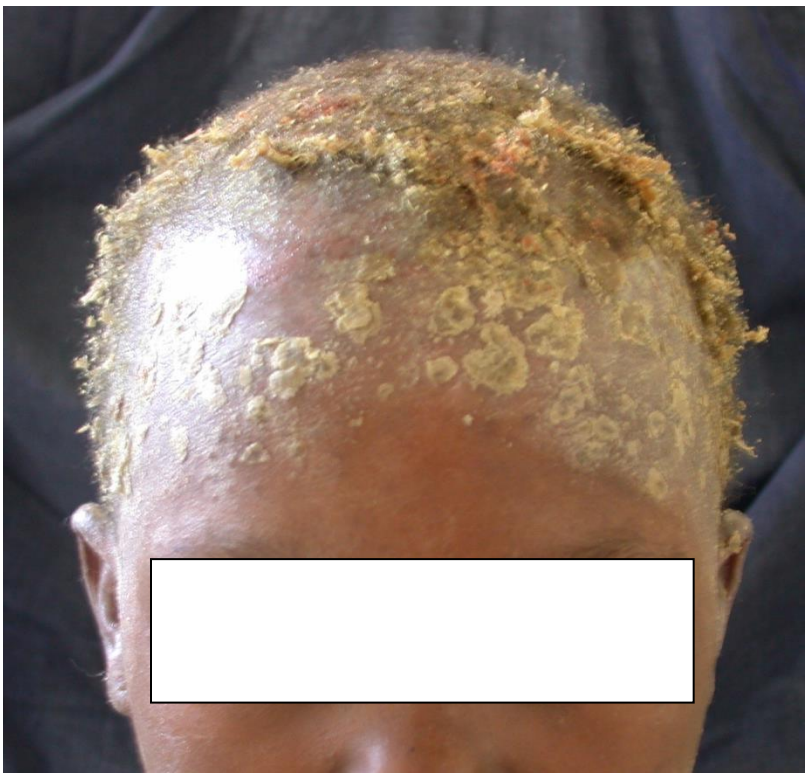

Figure 49: Pityriasis amiantacea, used sometimes to describe a severe form of seborrheic dermatitis.

Candidiasis

Description: Candidiasis is the most common opportunistic infection seen in HIV-infected children. It can affect the oral cavity, the oesophagus and the peri-anal region.

Aetiology: *Candida albicans* is the yeast responsible or candidiasis.

Clinical presentation: Oral candidiasis (thrush) occurs on the surface of the tongue, palate and buccal mucosa as white patches (plaques). This can be distinguished from milk curds by scraping the surface of the plaque, which results in erythema and point bleeds. Pseudomembranous candidiasis manifests as creamy white-to-yellow oral plaques. Atrophic candidiasis manifests as distinct areas of erythema with the loss of tongue papillae if the tongue is affected. Hyperplastic candidiasis (with both erythematous and white mucosal coloration symmetrically distributed) and angular cheilitis are other clinical variants of candidiasis.

Oral thrush can be seen in neonates and in patients receiving prolonged antibiotics and systemic steroids. Oesophageal candidiasis presents with dysphagia, odynophagia and retrosternal pain. Diaper rash due to candidiasis is usually red with a clearly defined border and consists of small red spots close to the large patches (satellite lesion). Diaper rash lasting for 3 days or longer may be candidiasis. *Candida albicans* is one of the causes of onychomycosis. In severely immunocompromised children the organism can cause candidemia or invasive candidiasis.

Epidemiology: Candida albicans is the most common cause of mucosal and oesophageal candidiasis. Oral thrush and diaper dermatitis occur among 50%-85% of HIV-infected children.

Diagnosis: Candidiasis is a clinical diagnosis which can be confirmed by a potassium hydroxide preparation and culture. Cobblestoning appearance on barium swallow may be seen in oesophageal candidiasis.

Prevention: In the mouth, for instance, this involves frequent toilet in the seriously ill, and denture hygiene in other patients, whereas in *Candida* infections affecting the skin, careful drying of affected sites is important.

Treatment: In many cases, topical antifungal therapy alone is sufficient to control the disease. Effective topicals include clotrimazole, nystatin and amphotericin B. Systemic therapy with fluconazole, itraconazole or amphotericin B is indicated in oesophageal disease. In addition, oral antifungals are used to prevent systemic candidiasis in severely immunocompromised patients. Clotrimazole troches or lozenges are used at 50mg 5 times a day while fluconazole and itraconazole dosing are 3-12mg/kg/day and 5mg/kg/day respectively.

Children with severe oral involvement due to diffuse and persistent candidiasis resistant to conventional treatment also tend to have feeding difficulties that may be related to oesophageal involvement. In these cases, the only effective therapy is intravenous fluconazole or amphotericin B.

Complications: Haematogenous dissemination of disease and invasive candidiasis can occur, resulting in candidemia, meningitis, endocarditis, renal disease, endophthalmitis, and hepatosplenic disease.

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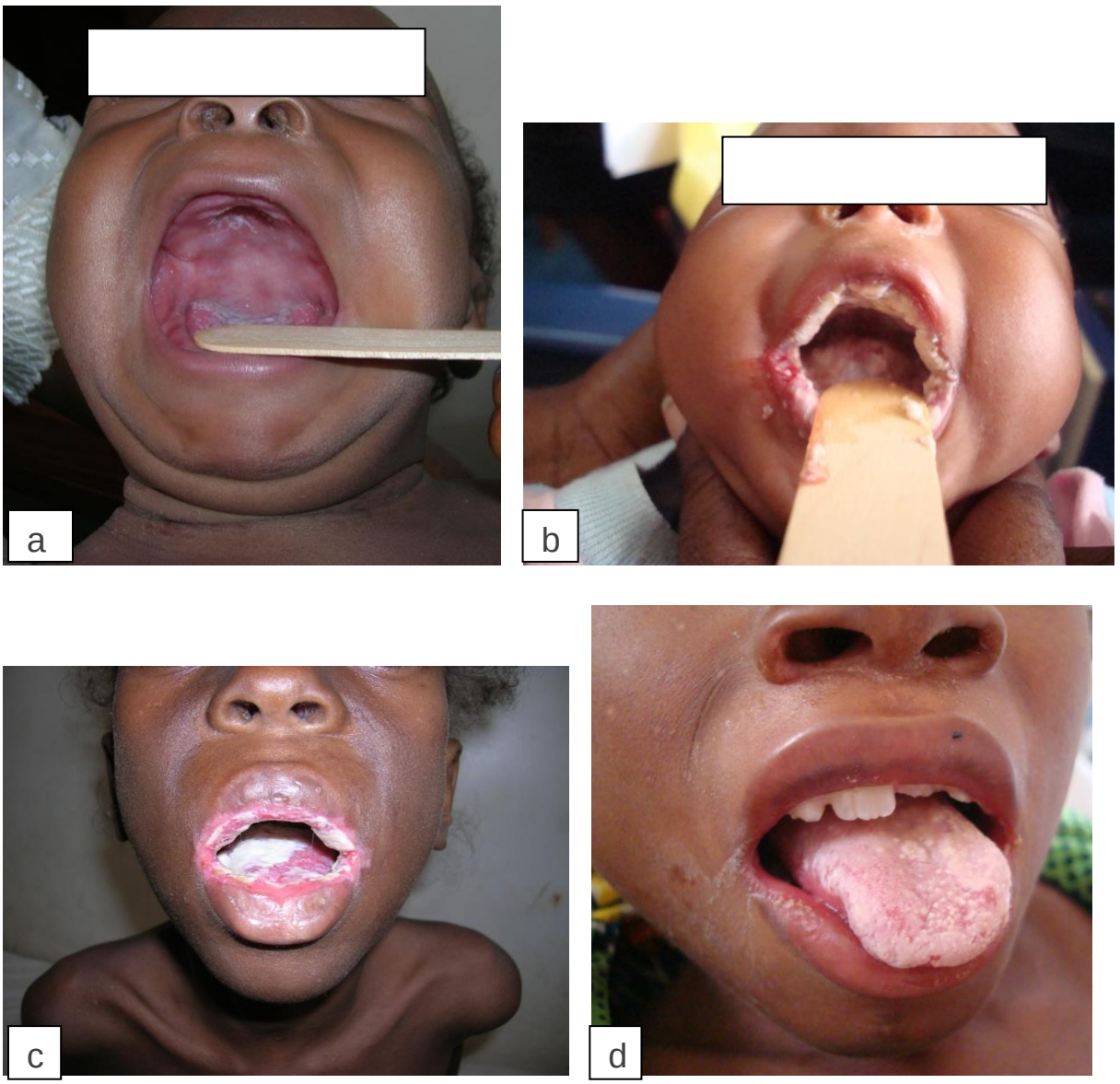

Figure 50a, b, c, and d: Oral candida in immunosuppressed children. Affecting the tongue and palate in (a), severe form in (b) and (c) and pseudomembranous variant in (d).

Anogenital Candidiasis

C. albicans is commonly isolated from the moist skin of the buttocks and genitalia of the infant but is more prevalent where the skin is affected by napkin rash. Satellite lesions may be seen.

Diagnosis: moistened swab or a scraping may be taken to discover whether or not *Candida* is present on the affected skin. If *Candida* is present, a trial of anti-candida therapy is indicated.

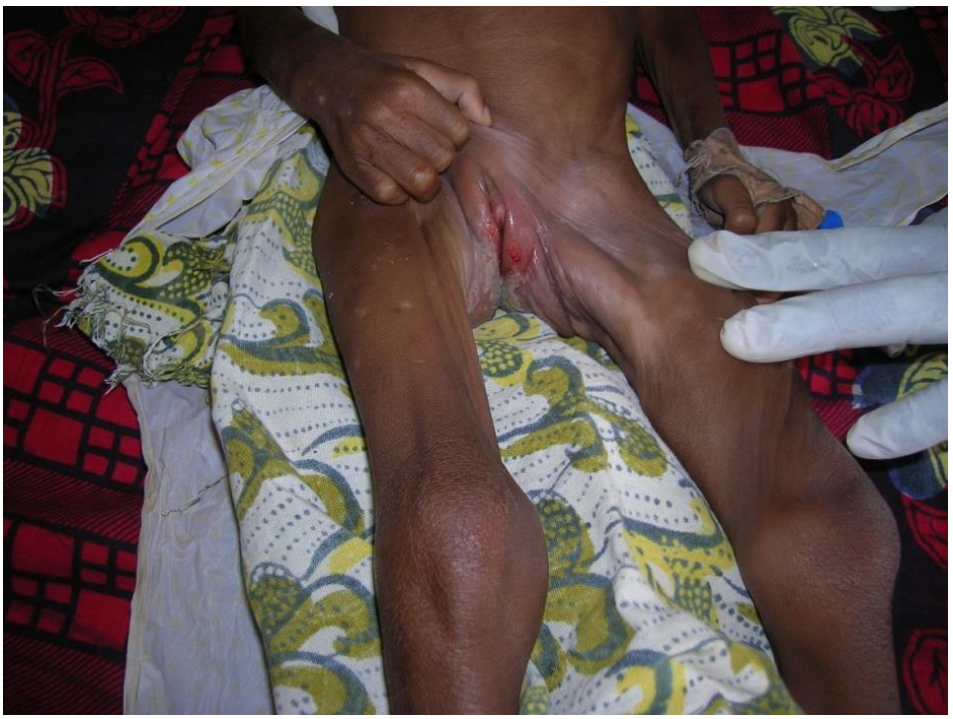

Figure 51: 2-year-old girl with severe pruritus vulva from vaginal candidiasis

Deep Fungal Infections

Histoplasmosis

Description:

Aetiology: Histoplasmosis is a fungal infection caused by the dimorphic fungus Histoplasma capsulatum.

Clinical presentation: Histoplasmosis is mainly inhaled and usually presents as a disseminated disease. Localized infections are rare. Skin may be the most frequent site of localised infection.

The cutaneous lesions of histoplasmosis are polymorphous and include papules, plaques, which may be crusted, erosions, ulcers, exanthems, nodules, acneiform eruptions, exanthems, molluscum-like lesions, acneiform folliculitis, psoriasiform eruptions, panniculitis, hyperkeratotic plaques, vasculitic lesions, erythema multiforme-like lesions, exfoliative dermatitis, abscesses and cellulitis. Oral ulcers and erosions are the most common manifestation of disseminated disease. There may be associated systemic symptoms including fever, lymphadenopathy, hepatosplenomegaly, lung disease and pancytopenia.

Diagnosis: Chest X-rays, tissue biopsies for histology and culture aid diagnosis. *Histoplasma capsulatum* can be identified on skin biopsy by the Gomori methenamine silver stain however culture of the organism is the gold standard.

Treatment: In addition to ART, infected patients benefit from systemic antifungal treatment with itraconazole or amphotericin B with long-term prophylaxis. For disseminated infection, the preferred approach is to give IV amphotericin for 4 weeks followed by itraconazole prophylaxis.

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Figure 52: Multiple lesions seen in the face of this child with histoplasmosis based on histopathology. Note nodules with hyperkeratotic centres, some of which seem umbilicated.

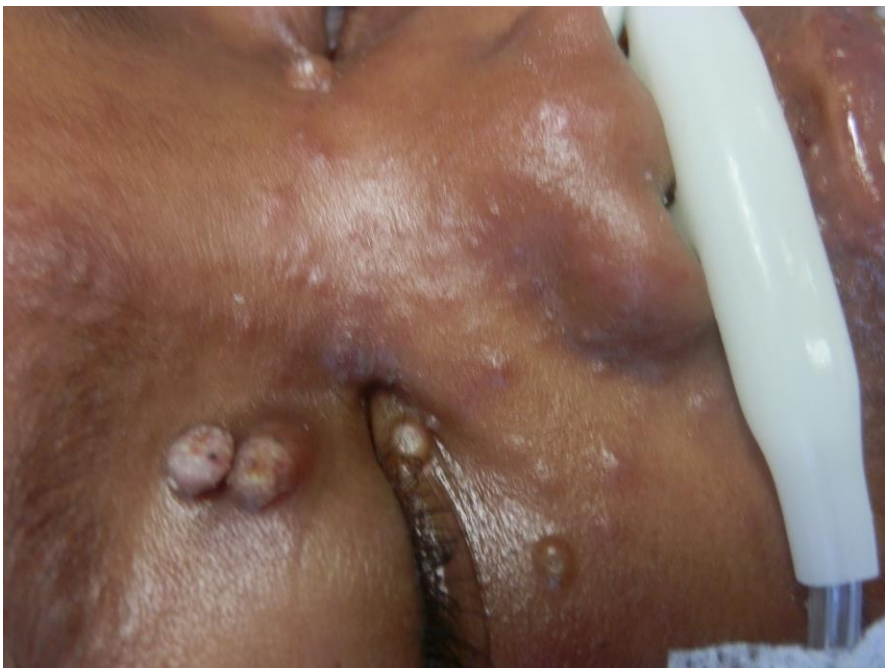

Figure 53: Close up photograph showing the same lesions as described above. Numerous erythematous papules widespread on the trunk of the same child as above with histoplasmosis, together with scarring from previous lesions.

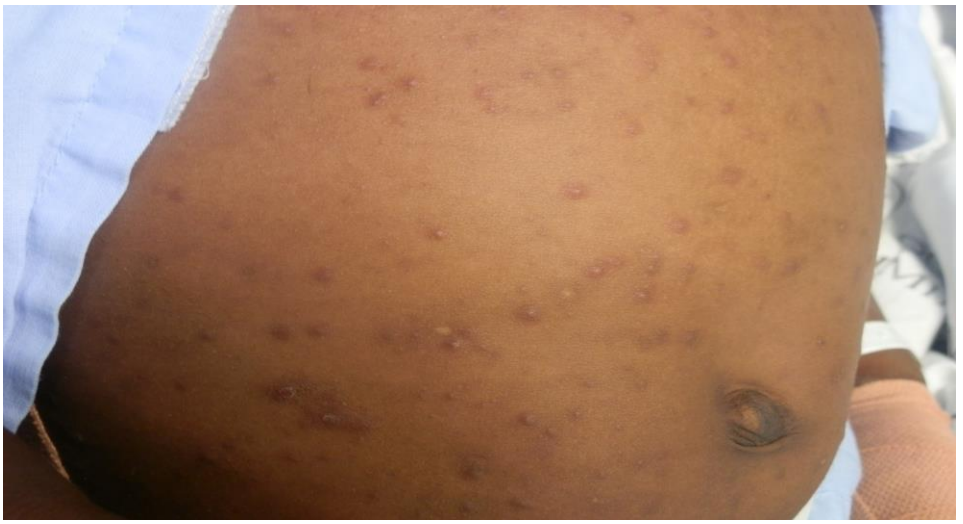

Figure 54: Numerous erythematous papules widespread on the trunk of the same child as above with histoplasmosis, together with scarring from previous lesions.

Figures 52 – 54 above emphasize the polymorphous nature of histoplasmosis lesion.

Cryptococcal Infection

Aetiology: Cryptococcosis is caused by *Cryptococcus neoformans.*

Clinical presentation: Brain, lung and skin are sites of predilection. In the skin, it presents as jelly-like necrotizing papules and nodules that resemble molluscum contagiosum. Acneiform, tumourous (warty) and papulopustular variants of the disease have been documented.

Epidemiology: Before the advent of ART, was estimated to affect 5-10% of persons with AIDS in the US and UK, and 30-40% in Africa.

Diagnosis: For systemic disease, serology, blood culture, urine culture and lumber culture should be done. Cutaneous disease can be confirmed by skin biopsy with special stains for the cryptococcal capsule and culture or Tzanck smear.

Treatment: Intravenous amphotericin B and oral fluconazole (see cryptoccocal infection in Part 2 of the atlas). Secondary prophylaxis is with fluconazole.

Further reading

1. Ricchi E, Manfredi R, Scarani P et al. Cutaneous cryptococcosis and AIDS. J Am Acad Dermatol 1991; 25: 335–6.
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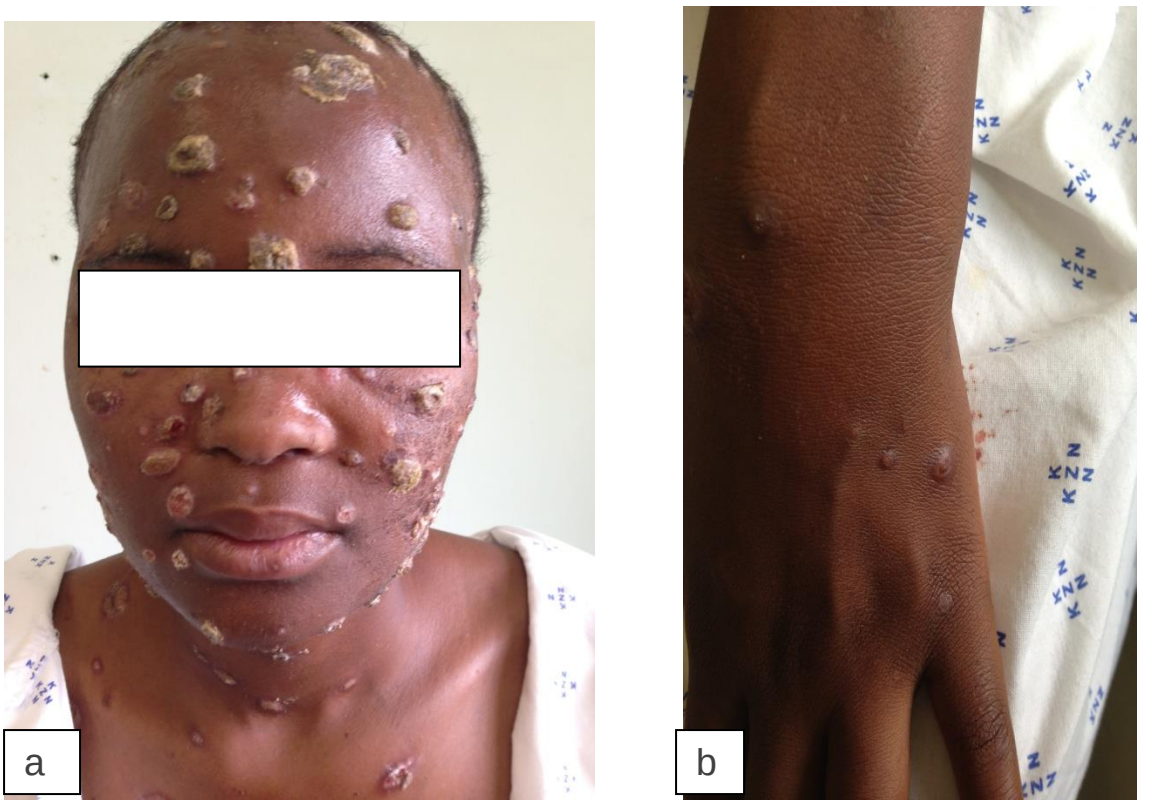

Figure 55a and b: Cutaneous cryptococcosis (Courtesy of Prof. Anisa Mosam. Dermatology Department, University of Kwazulu Natal).

Emergomyces Africanus (Formerly Emmonsia) Infection

A recent report of cases of a new species of dimorphic fungus pathogenic to humans, especially in human immunodeficiency virus-infected was made in South Africa adults, most of whom presented with lung and skin lesions. A case of disseminated emmonsiosis has also been reported in an HIV-infected child. The child had severe immunosuppression (CD4+ T cell count 0.012 x 10^9/L). The DNA sequence was identical to the disseminated disease caused by the novel organism. Many of these cases of emergomycosis had initially been diagnosed as histoplasmosis.

Aetiology: Causative organism: closely related to Emmonsia pasteuriana now called Emergomyces africanus.

Treatment: Amphotericin B given for 6 weeks, in addition to initiation of ART.

Further reading

1. Kenyon C, Bonorchis K, Corcoran C, et al. A dimorphic fungus causing disseminated infection in South Africa. N Engl J Med 2013; 369 (15): 1416–1424.
2. Lochan H, Naicker P, Ryan A et al. A case of disseminated emmonsiosis in an HIV-infected child. Southern African HIV Clinician Society Conference; 24-27 Sept 2014.
3. Schwartz IS, Govender NP, Corcoran C, Dlamini S, Prozesky H, Burton R, Mendelson M, Taljaard J, Lehloenya R, Calligaro G, Colebunders R, Kenyon C. Clinical Characteristics, Diagnosis, Management, and Outcomes of Disseminated Emmonsiosis: A Retrospective Case Series. Clin Infect Dis. 2015 Sep 15;61(6):1004-12.

Sporotrichosis

Background: A deep fungal infections more common in adults affected with HIV than children. In immunocompetent individuals, infection generally results from cutaneous inoculation by trauma it may present as a disease of the skin and draining lymphatics. Sporotrichosis associated with HIV may in addition occur as pulmonary infection following spore inhalation and may be haematogenously spread from pulmonary infection to the skin and joints.

Aetiology: The agent, *Sporothrix schenckii*, a dimorphic fungus found in soil and in animal faeces, is responsible for most infections.

Epidemiology: Sporotrichosis is relatively uncommon even though it shares a worldwide distribution. In some parts of the world, the condition follows cat scratch or contact with the affected animal's wound.

Diagnosis: Tissue biopsy and fungal culture are the mainstay of diagnosis. Blood culture samples, bronchoalveolar lavage or CSF for microscopic examination may be helpful.

Clinical: On the skin, sporotrichosis presents as suppurating nodules that progress onto ulcers at the point of inoculation and progress proximally along lymphatic vessels. In disseminated disease the skin lesions are widespread.

Other organs can be affected in visceral disease including the CNS, joints, spleen, bone marrow, pneumonia, meningitis and eyes

Treatment: Amphotericin B at a dose of 0.7mg/kg per day for 3 to 4 weeks. Potassium iodide, normally used for infected patients is not recommended for HIV/AIDS patients. Other options include itraconazole and fluconazole.

Further reading

1. Carvalho MT, de Castro AP, Werner BB et al. Disseminated cutaneous sporotrichosis in a patient with AIDS: report of a case. Rev Soc Bras Med Trop, 35 (2002) 655–659S.
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3. Edwards C, Reuther WL, Greer DL. Disseminated osteoarticular sporotrichosis: treatment in a patient with acquired immunodeficiency syndrome. South Med J, 93 (2000), 803–806.
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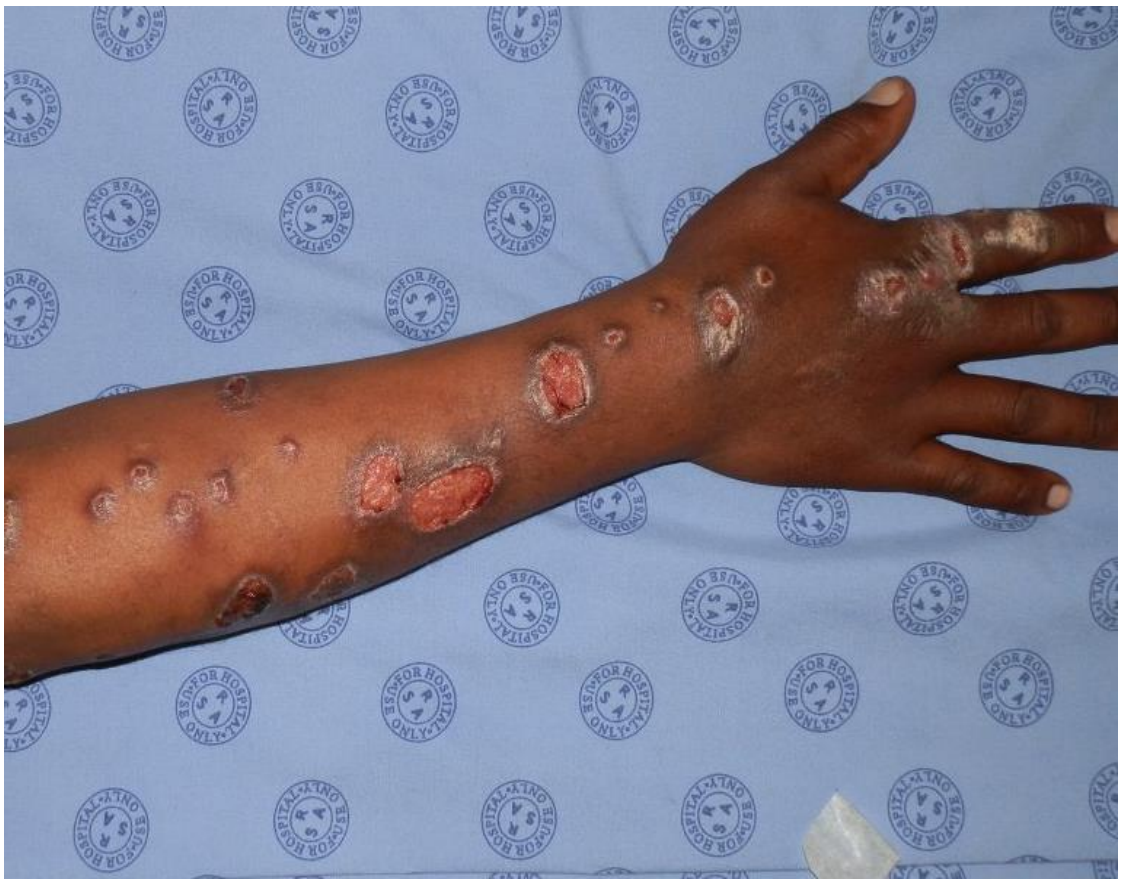

Figure 56: Sporotrichosis on the arm of an HIV-infected child. Note the predominantly linear "sporotrichoid spread" along the lymphatics.

Table 3: Fungal Infections – Treatment options

Condition	First line	Second line	Where available/ indicated
Superficial fungal infections			
Tinea Corporis	Topical agents: including clotrimazole, econazole, oxiconazole, miconazole, terbinafine, naftifine	Oral griseofulvin	Terbinafine, itraconazole, fluconazole
Tinea Capitis	Oral Griseofulvin 10mg/kg daily x 6 weeks	Fluconazole-6mg/kg once weekly for 6 weeks	Oral terbinafine, itraconazole
Candidiasis	Topical clotrimazole, nystatin	Clotrimazole troches	Severe infection - systemic agents: fluconazole, itraconazole, amphotericin B
Pityriasis versicolor	-20% sodium hyposulphite solution -2.5% selenium sulphide in a detergent base (Selsun® shampoo)	Ketoconazole shampoo, terbinafine 1% cream	Oral ketoconazole, itraconazole
Deep fungal infections			
Histoplasmosis	Oral itraconazole	Amphotericin B	
Cryptococcosis	Amphotericin B + Fluconazole	Fluconazole only	
Sporotrichosis	Amphotericin B	Itraconazole	Fluconazole

CHAPTER 4: SKIN INFESTATIONS

Scabies

Description: The clinical presentations of scabies include papular, nodular, bullous and crusted scabies.

Aetiology: Scabies is caused by a mite (*Sarcoptes scabiei var homini*) and has an incubation period of about three weeks.

Clinical presentation: Presents with Itching (severe at nights), characteristic burrow in the interdigital web spaces, papules, blisters, nodules, and eczematous changes. The skin lesions commonly involve web spaces, flexor surface of wrists, axillae, umbilicus, waist, feet, and ankles. In HIV-infected children it can affect the face, scalp and nail folds. Crusted or Norwegian scabies is mainly seen in immunosuppressed individuals such as patients with HIV/AIDS. It is highly contagious and may be the source of epidemics.

Epidemiology: An estimated 300 million cases per year occur worldwide. It is associated with overcrowding and poor sanitary conditions. Epidemics can occur among children in institutional care. Mode of transmission is mainly through direct contact.

Diagnosis: Clinical diagnosis can be made but definitive diagnosis is made by microscopic identification of mites, eggs, or mite faeces (scybala) from skin scrapings.

Prevention: Personal hygiene. Prompt diagnosis and effective treatment. Avoid close contact with infected persons or contaminated fomites.

Treatment: Treat the whole body and all contacts with scabicides. Where available, the commonly used scabicide is benzyl benzoate. If benzyl benzoate is not tolerated, sulphur ointment is used. For children <6months of age: 5% sulphur ointment twice daily for 3 days; 6 months – 2 years of age: ¼ strength benzyl benzoate as a single application; 2 – 12years of age: ½ strength benzyl benzoate as a single application and >12 years of age: full strength benzyl benzoate as a single application. Permethrin and ivermectin are alternative therapy: 200mcg/kg in two divided doses given 2 weeks apart. In crusted scabies oral ivermectin is best combined with a topical scabicide. It is useful to remember that the scabies mite can only live about 72 hours without human contact, but once on a person, the mites can live up to two months.

Tetmosol soap is added to wash the body, clothes and linen.

Complications: Secondary bacterial infection can occur.

Further reading

1. Gilmore SJ. Control Strategies for Endemic Childhood Scabies. PLoS One. 2011; 6(1): e15990.
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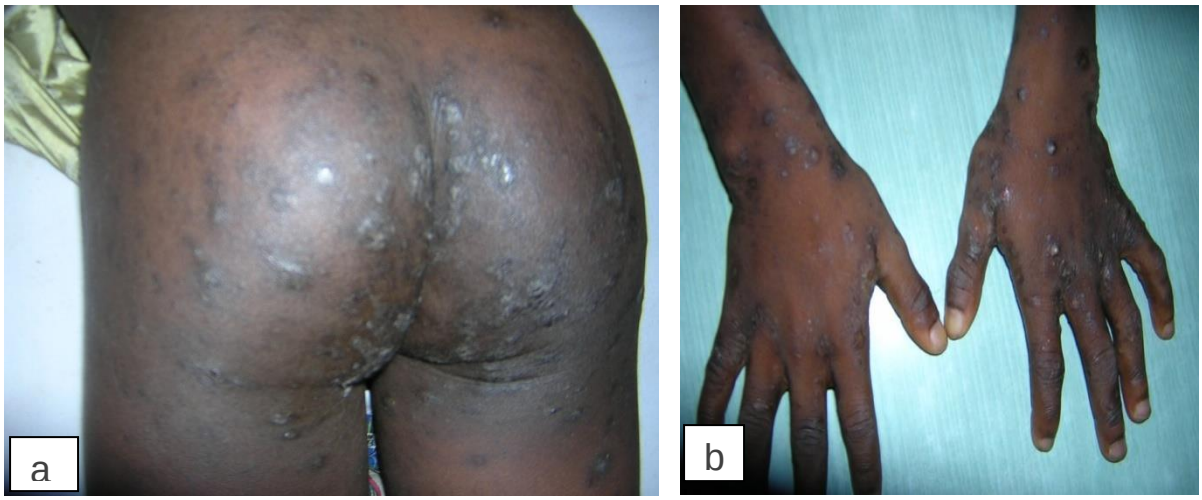

Figure 57: Scabies on buttock and hands, note web spaces involvement.

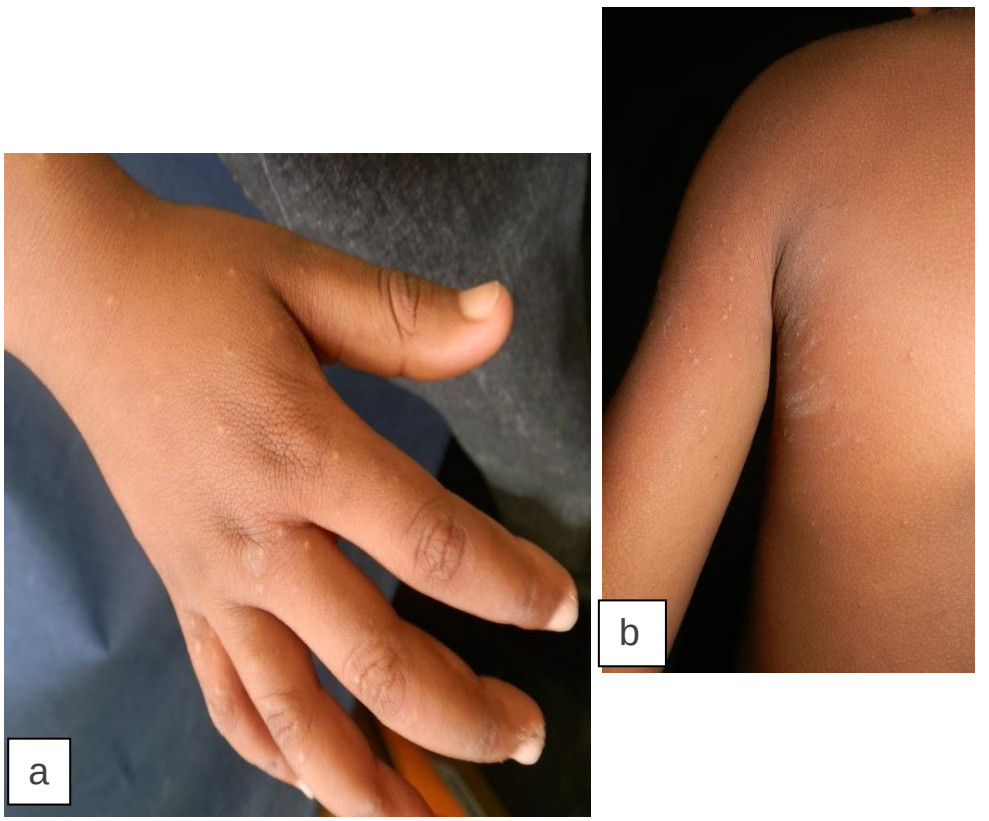

Figure 58a and b: Scabies: Note the interdigital distribution.

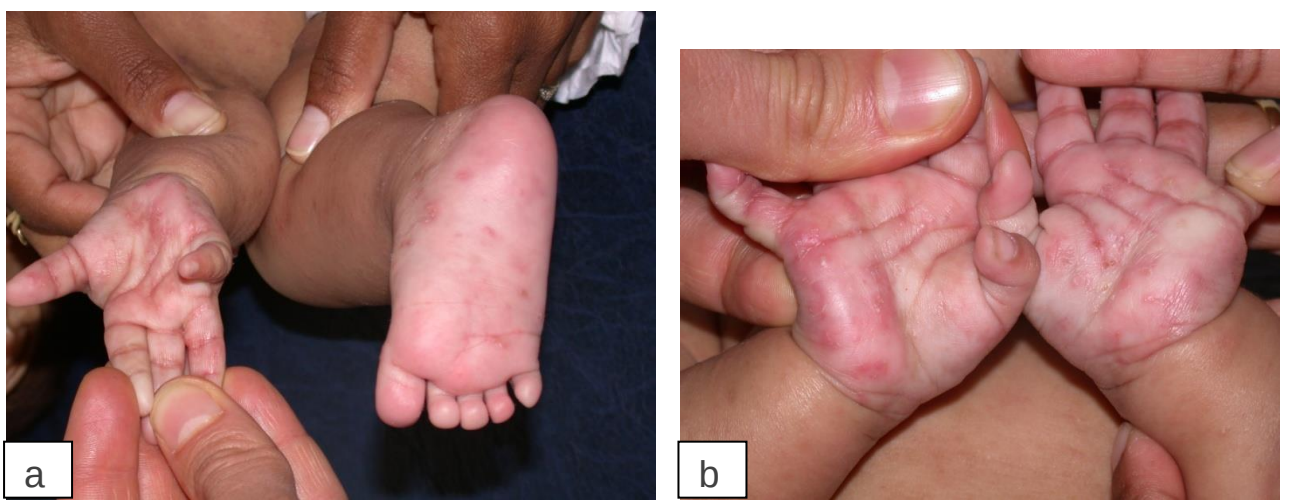

Figure 59a and b: Scabies on the sole and palms of an infant.

Pediculosis

Description: Pediculosis is infestation of the hairy parts of the body by lice.

Aetiology: Head lice are caused by *Pediculus humanus capitis* while pediculosis pubis causes infestation of the public area.

Clinical presentation: Itching on the affected area 3-4 weeks after infestation.

Epidemiology: A common parasitic infection in children and most prevalence in children between 3 and 11 years old. It is rare in African children due to the texture of their hair. There is no seasonal variation or relationship with the level of hygiene.

Diagnosis: Pediculosis is diagnosed by identifying live lice on the affected area.

Prevention: Health education. Avoid physical contact with infested persons and their materials such as beddings, clothing and comb.

Treatment: There is no modality that assures destruction of the eggs and hatched lice after a single treatment. Options include physical methods (wet combing), topical pediculicides (pyrethrins, pyrethroids pyrethrins, and lindane). Treatment should be repeated after an interval of 7-10 days. All other contacts should also be treated.

Complications: Secondary bacterial infections.

Further reading

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2. Leone P. Scabies and pediculosis pubis: an update of treatment regimens and general review. Clin Infect Dis. 2007; 44: S153-S159.

Figure 60a and b: Pediculosis capitis in a) and lice in b).

Myiasis

Description: Myiasis manifests as boil-like lesions, usually on exposed areas of the body such as the trunk, thigh and buttocks.

Aetiology: The lesions are caused by infestation of the skin by developing larvae (maggots) of the tumbu fly (*Cordylobia anthropophaga*). The female fly lays its eggs on dry, sandy soil or on damp clothing hung out to dry. The eggs hatch in 1 to 3 days and penetrate the skin.

Epidemiology: The tumbu fly is prevalent in sub-Saharan Africa, thriving in the warm and humid environment. Myiasis occurs more commonly in children and during the raining season.

Clinical presentation: Lesions can be painful, pruritic, and tender, and patients often have the sense of something moving under the skin. There may also be fever or swollen glands. In ophthalmomyiasis, there may be severe eye irritation, redness, foreign body sensation, pain, lacrimation, and swelling of the eyelids.

Diagnosis: Each lesion has a central punctum from which serosanguinous fluid may be discharged and the movement of the larva may be noticed by the patient. The tip of the larva may protrude from the punctum. Diagnosis is typically made by identification of the larvae. Ultrasonography may be useful in establishing the diagnosis and in determining the size of the larvae. Biopsies are not usually necessary.

Treatment: A non-invasive mode of management is to occlude and suffocate the larva by application of petroleum jelly or liquid paraffin over the central punctum. This makes the larvae to emerge spontaneously head-first over the course of several hours, at which time, tweezers (or forceps) aid in the removal.

Prevention: Clothing should be hot-ironed and dried appropriately to remove any residual eggs in areas endemic to tumbu flies.

Further reading

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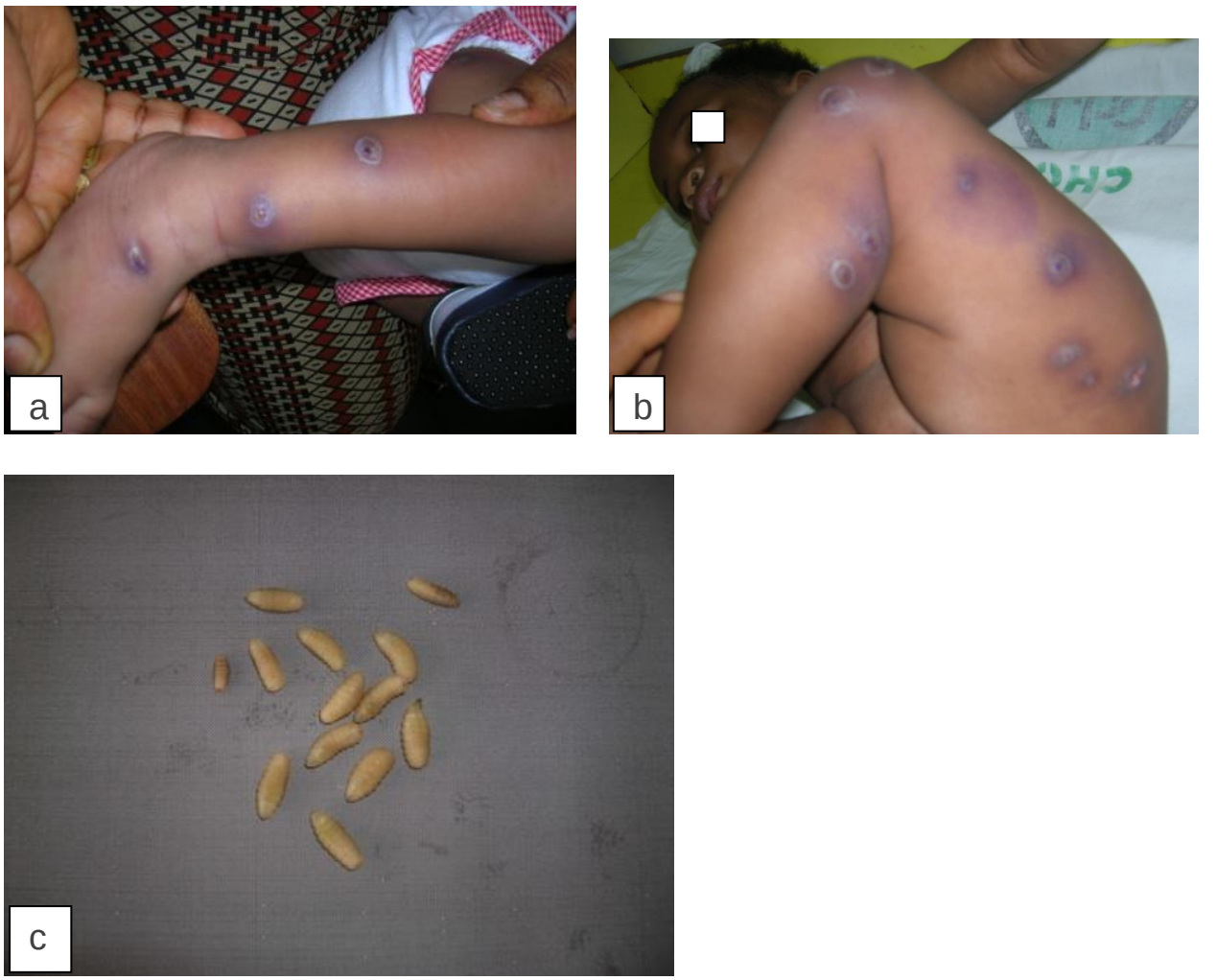

Figure 61a, b and c: Myiasis involving the lower limbs in a 6-month-old girl seen in the clinic (a), (b). The larvae (c) were expressed from the lesions.

Table 4: Parasitic infections – Treatment options

Condition	Treatment1	Treatment2	Treatment3
Scabies	Benzyl benzoate	Ivermectin	Permethrin
Pediculosis	Physical methods (wet combing)	Choice of pyrethrins, pyrethroids, lindane	Oral antihelminthics and antibiotics
Myaisis	Petroleum jelly or liquid paraffin over the central punctum		

CHAPTER 5: INFLAMMATORY SKIN CONDITIONS

The most common conditions in this group are seborrheic dermatitis, xerosis and papular eruptions.

Moisturisers and emollients may be useful in certain conditions discussed in this section. They help sooth and hydrate the skin and include oil instilled in the baths (e.g. liquid paraffin) and creams (e.g. Cetomacrogol cream). Lotions and ointments (emulsifying ointment or humectants such as 5-10% Urea contained in emulsifying ointment) are also available to be applied directly to the skin but are reserved for applications to very dry skin.

Topical corticosteroids (applied to the skin as cream or ointment) used as anti-inflammatory agents are subdivided into seven groups, with group one being the most potent and group seven the least potent *(WHO model prescribing information- Drugs used in skin diseases. Geneva, World Health Organization, 1997).*

Group 1: Super high potency e.g. clobetasol propionate 0.05%.

Group 2: High potency e.g. betamethasone diproprionate 0.05%.

Group 3: Upper-mid potency e.g. mometasone furoate 0.1% ointment.

Group 4: Mid potency e.g. mometasone furoate 0.1% cream.

Group 5: Lower-mid potency e.g. betamethasone valerate 0.1%.

Group 6: Mild potency e.g. fluocinolone acetonide 0.01%.

Group 7: Least potent e.g. hydrocortisone 1%.

Papular Urticaria

Definition: Recurrent and often chronic hypersensitivity reaction to insect bites.

Aetiology: The reaction results from mosquito, flea, bedbug and other insect bites in hypersensitized children.

Epidemiology: Papular urticaria is predominantly a disease of children although it also occurs in non-local adults. It is thought to affect adults who have not been desensitized by previous recurrent bites by the same insects. It is a self-limiting condition and the children tend to outgrow the disease.

Clinical presentation: It presents as intensely pruritic papules that may be surrounded by a wheal. In severe cases blisters may form. The lesions tend to occur in groups or clusters in exposed and covered parts of the body. Scratching may result in excoriation and dyspigmentation. In recurrent cases, the lesions are usually in different stages of evolution.

Diagnosis: Papular urticaria is a clinical diagnosis. A skin biopsy is helpful in supporting the diagnosis in difficult cases.

Prevention: Insect repellents and insecticides help prevent insect bites

Treatment: This is mainly symptomatic and topical steroids (e.g. 1% Hydrocortisone cream) and antihistamines (e.g. Chlorpheniramine) are helpful**.**

Complications: secondary bacterial infections

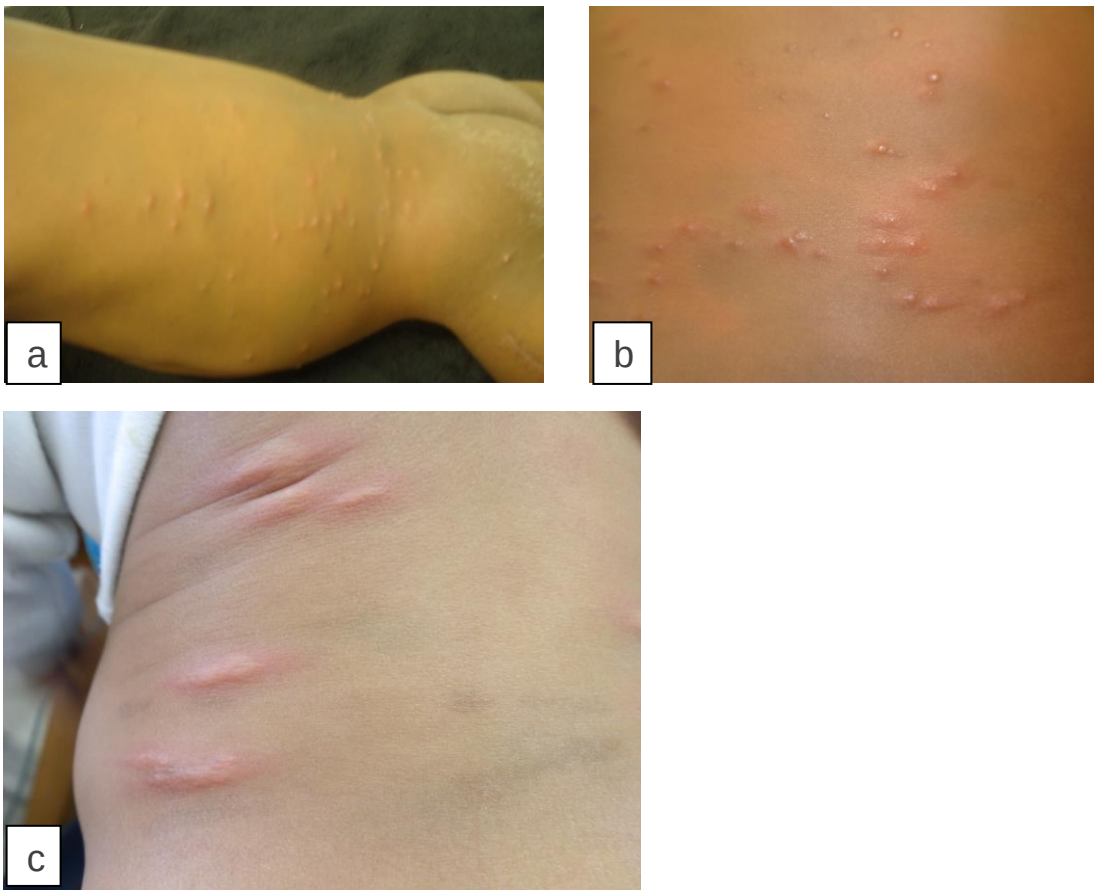

Figure 62a, b and c: Papular urticaria. Note the urticarial plaques in (a), (b) and blisters in (c).

Papular Pruritic Eruption of HIV (PPE)

HIV-related pruritic papular eruption (PPE) and eosinophilic folliculitis (EF) are poorly differentiated and are confused in their diagnosis.

Description: Papular pruritic eruptions (PPE) are a common dermatological manifestation of HIV and may often be the may often be the first sign of HIV which could be useful in diagnosing the infection. PPE is a sign of advanced degree of immunosuppression, occurring at low CD4 T-cell counts. The severity of PPE increases as CD4 counts decrease.

PPE has a clinical overlap with eosinophilic folliculitis (EF) of HIV.

Epidemiology: PPE prevalence varies between 10 and 60% depending on geographical area. It is common in Africa and Asia.

Aetiopathogenesis: PPE is postulated to be due to altered and exaggerated immune response to arthropod antigens as a result of the increased involvement of exposed or uncovered skin. It is associated with eosinophilia and elevated IgE.

Clinical presentation: PPE presents as chronic waxing and waning, intensely pruritic papules and symmetric involving predominantly the extremities and trunk, though facial involvement can also occur. The mucous membranes, palms and soles are spared. Extensive excoriation with subsequent scarring and post-inflammatory hyperpigmentation from scratching and infection can be disfiguring and stigmatizing.

Diagnosis: Skin biopsy is helpful to diagnose both EF and PPE. PPE histology shows a wedge-shaped, moderately dense, superficial and deep perivascular and interstitial lymphocytic and eosinophilic infiltrate; the epidermis is hyperplastic and there may be a spongiotic punctum.

Differential diagnosis: Differential diagnosis of both PPE and EF include nodular prurigo, prebullous pemphigoid, scabies, papulonecrotic tuberculid, drug eruption, photodermatitis, secondary syphilis, onchodermatitis and eosinophilic, pityrosporum, bacterial and acneiform folliculitis.

Treatment: It is a strong clinical indication for initiating ART. Initiation of ART has been shown to dramatically decrease the severity of PPE-HIV, often with lesions disappearing and not returning. Treatment of PPE is similar to that of eosinophilic folliculitis. Topical steroids, antihistamines, phototherapy and pentoxifylline (oxpentifylline) have been claimed to be efficacious.

Eosinophilic folliculitis (EF)

EF is common among HIV-infected children. It is a marker of CD4 decline. The cause of EF is unknown. It is thought to be a result of immune dysregulation to a variety of agents such as

Pityrosporum ovale, or the follicular mite *Demodex folliculorum*, an autoimmune reaction to the sebocyte, or a component of sebum.

Clinical presentation: EF has characteristic morphology and distribution, resembling insect bites. EF presents as a centripetal (face and trunk) eruption of pruritic, erythematous, perifollicular papules and pustules. Patients with eosinophilic folliculitis may be subclinically photosensitive. It manifests as discrete erythematous papules, or papules surmounted by a tiny pustule concentrated on the face, neck, upper trunk and proximal part of the upper limbs. It is usually itchy and may be difficult to differentiate from papular pruritic eruption.

Diagnosis: Skin biopsy for EF characteristically shows degranulating eosinophils and mast cells in a perifollicular distribution. Blood tests may be useful in EF as there may be a peripheral eosinophilia.

Treatment: For EF institution of ART is critical. The first line of treatment is topical steroids, emollients, and oral antihistamines. Phototherapy is the most successful treatment modality but other treatments that have been tried including topical disodium cromoglycate, topical tacrolimus, oral antibiotics (erythromycin, tetracyclines, co-trimoxazole), oral itraconazole (for its anti-eosinophilic effect), oral dapsone, oral indomethacin, oral isotretinoin and oral metronidazole with antipruritic agents.

Prevention: The lesions can be reduced by covering the extremities to reduce exposure to insect bites.

Complications: Secondary bacterial infections.

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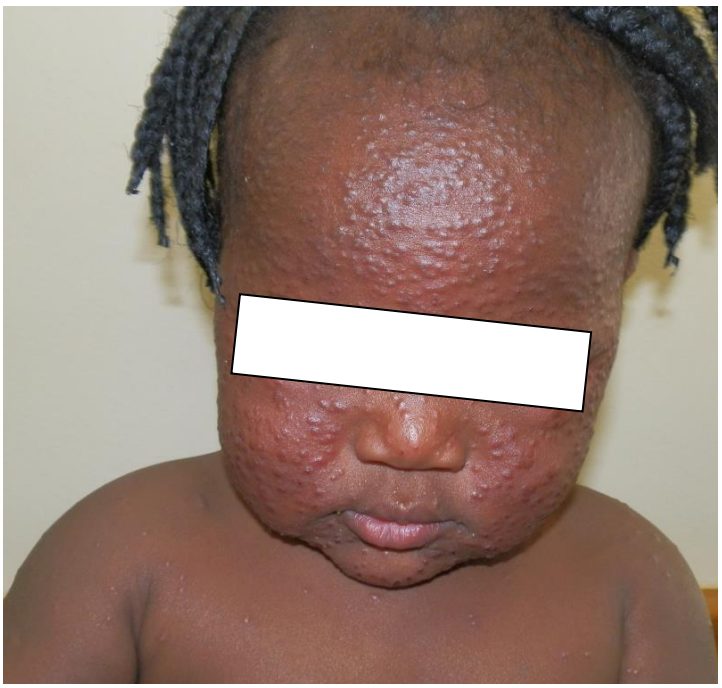

Figure 63: Eosinophilic folliculitis – multiple monomorphous papules of on the face of an HIV-infected child.

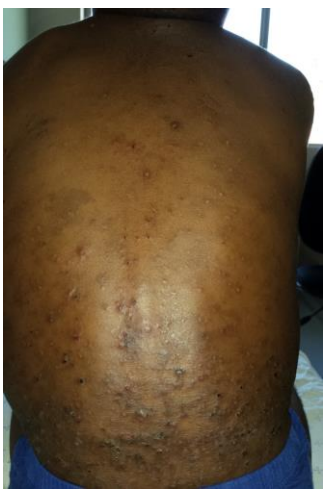

Figure 64: Papular pruritic eruptions (PPE) presenting with widespread papules, excoriations, some with crusted centres concentrated on the lower back.

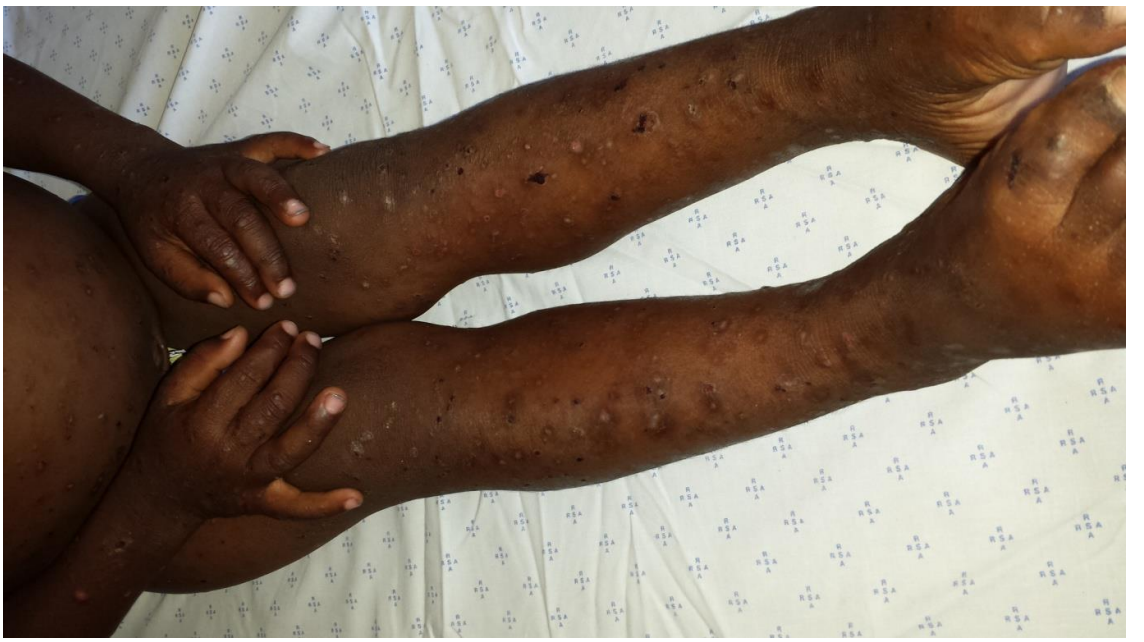

Figure 65: PPE- Widespread excoriated papules on the lower abdomen, dorsum of the hands and lower limbs.

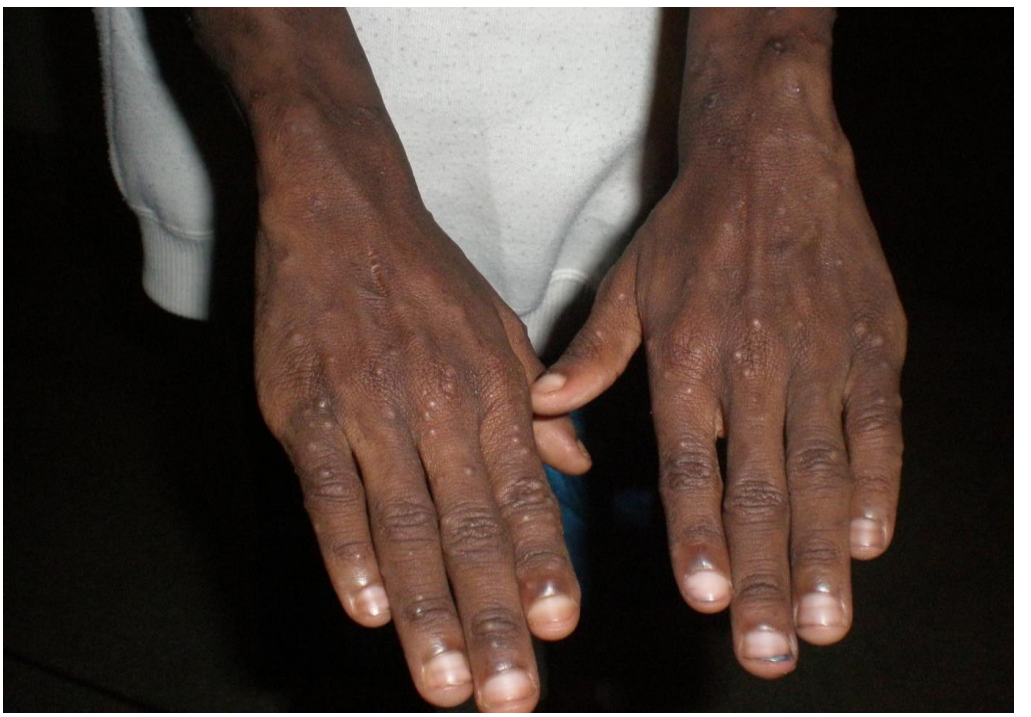

Figure 66: PPE in an HIV-infected adolescent: There were excoriated, erythematous, urticarial papules on the hand and trunk of this patient before initiation of ART.

Sebborrheic Dermatitis

Description: An inflammatory condition that is characterized by chronic and recurrent erythema and greasy scale in areas with terminal hairs and large sebaceous glands. There are two types: infantile and adult types.

Aetiology: The disease is thought to be related to overgrowth or abnormal or exaggerated immune response to *Malassezia* species (*Pityrosporum* yeasts). Sebaceous gland secretion, presence of *Malassezia* yeast, and the host immune response combine to play role in the pathogenesis of this skin condition.

Clinical presentation: Erythema, greasy scale, may also appear as macules or plaques with dry white or crusts or moist oily scale.

Epidemiology: Seborrheic dermatitis is the most common inflammatory dermatoses in HIV-infected children. The infantile type is self-limiting within the first few months of life while the adult type appears around the time of puberty. It affects the scalp, face (nasolabial folds and eyebrows), chest and body folds. The prevalence among HIV-infected individuals is about 40% and as high as 80% among AIDS patients.

Diagnosis: It is a clinical diagnosis, but fungal infection should be excluded with a negative potassium hydroxide test. Histologically, the lesions of seborrheic dermatitis in patients without HIV-1 are those of eczema; however, with chronicity tend to resemble those of psoriasis. Thus, in longstanding cases it may be difficult to differentiate seborrheic dermatitis from psoriasis, both clinically and histologically.

Treatment: Treatment options include topical steroids, antifungals and emollients. The scalp can be treated by washing daily with shampoos containing selenium sulphide, ketoconazole, zinc pyrithione, salicylic acid or coal tar.

Crusts or scales can be removed by overnight application of salicylic acid in water-soluble bases such as aqueous cream. Corticosteroid scalp applications or creams, with or without 2% precipitated sulphur, may alleviate erythema and itching.

For the face, low-potency corticosteroids such as 1% hydrocortisone are usually sufficient. These may be mixed with 2% precipitated sulphur or with an imidazole, as in some proprietary compounds. For the flexures, imidazole and hydrocortisone mixtures are best.

Treatment of the trunk usually requires potent topical corticosteroids. Oral itraconazole, which has activity against *Malassezia*, may be used at a dose of 100 mg for up to 3 weeks, and may result in long-term remission in some patients. Lithium succinate 5% cream with or without hydrocortisone has been useful in some cases.

Complications: Secondary infection with bacteria (*staphylococcus aureus*) or viruses (HSV-1).

Further reading

1. Gary G. Optimizing treatment approaches in seborrheic dermatitis. J Clin Aesthet Dermatol. 2013; 6(2): 44–49.
2. Filiberto Cedeno-Laurent F, Gómez-Flores M, Mendez N et al. New insights into HIV-1-primary skin disorders. J Int AIDS Soc. 2011; 14: 5.
3. Mathes BM, Douglass MC. Seborrheic dermatitis in patients with acquired immunodeficiency syndrome. J Am Acad Dermatol. 1985;14:947–951. doi: 10.1016/S0190-9622(85)70243-5.
4. Froschl M, Land HG, Landthaler M. Seborrheic dermatitis and atopic eczema in human immunodeficiency virus infection. Semin Dermatol. 1990; 14:230–232.
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7. Stefanki C, Alexander J, Stratigos JD. Skin manifestation of HIV in children. Clin Dermatol 2002; 20; 74-86.

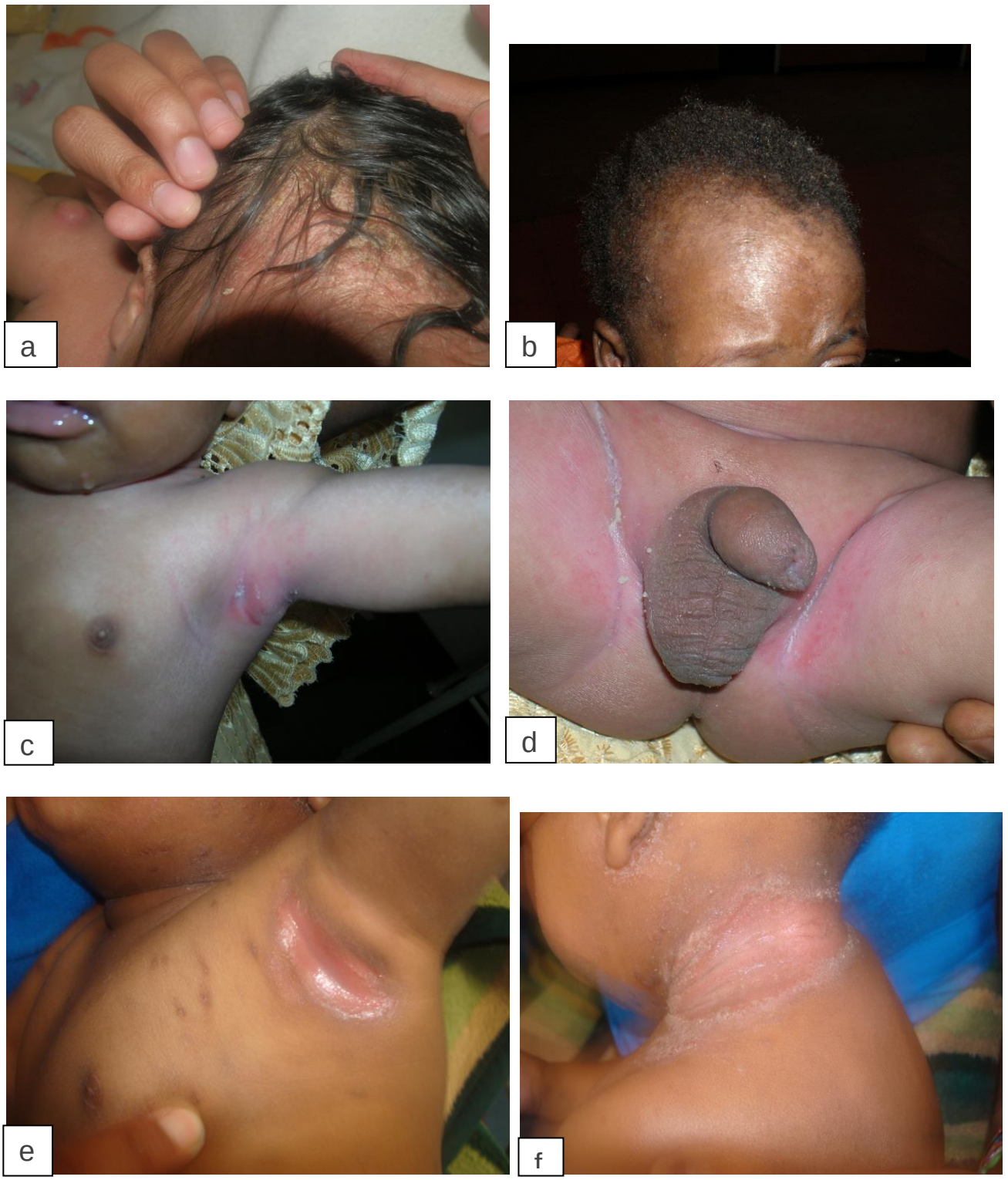

Figure 67a, b, c, d, e and f: Seborrheic dermatitis in young children affecting the scalp, neck, perineum and axilla.

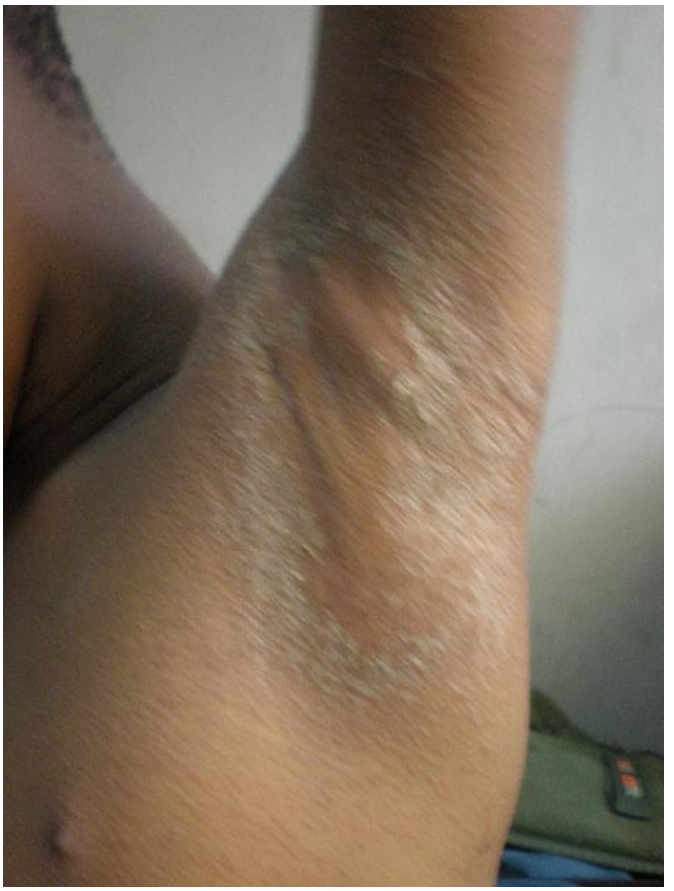

Figure 68: Seborrheic dermatitis in the axilla of an older child. Note the central exudation, scaling at the periphery.

Atopic Dermatitis

Description: A chronic skin condition characterized by xerosis, pruritus, and inflammation.

Aetiology: Unclear but "hygiene hypothesis" and the "keratinocyte apoptosis hypothesis" have been proposed. Interactions among genetic, environmental, skin barrier, immune factors, and stress are documented. Symptoms may be exacerbated by allergic reaction to several triggers.

Clinical presentation: Dryness of skin, itch, typical distribution all in a background of positive family history.

Epidemiology: Common among HIV-infected children. The risk of atopic dermatitis was increased by 30% in one study.

Diagnosis: Atopic dermatitis is a clinical diagnosis.

Prevention: There are no specific preventative measures but as in non-infected persons, avoidance of triggers, ensuring that the skin is always well moisturized is helpful.

Treatment: Avoid triggers. Use emollients, steroids and topical immune response modifiers such as tacrolimus.

Complications: Secondary bacterial infections.

Further reading

1. Gary G. Optimizing treatment approaches in seborrheic dermatitis. J Clin Aesthet Dermatol. 2013; 6(2): 44–49.
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3. Pastar Z, Lipozencić J, Ljubojević S. Etiopathogenesis of atopic dermatitis--an overview. Acta Dermatovenerol Croat. 2005;13(1):54-62.
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5. Siberry GK, Leister E, Jacobson D. Increased risk of asthma and atopic dermatitis in perinatally HIV-infected children and adolescents. Clin Immunol. 2012; 142 (2): 201 -208.

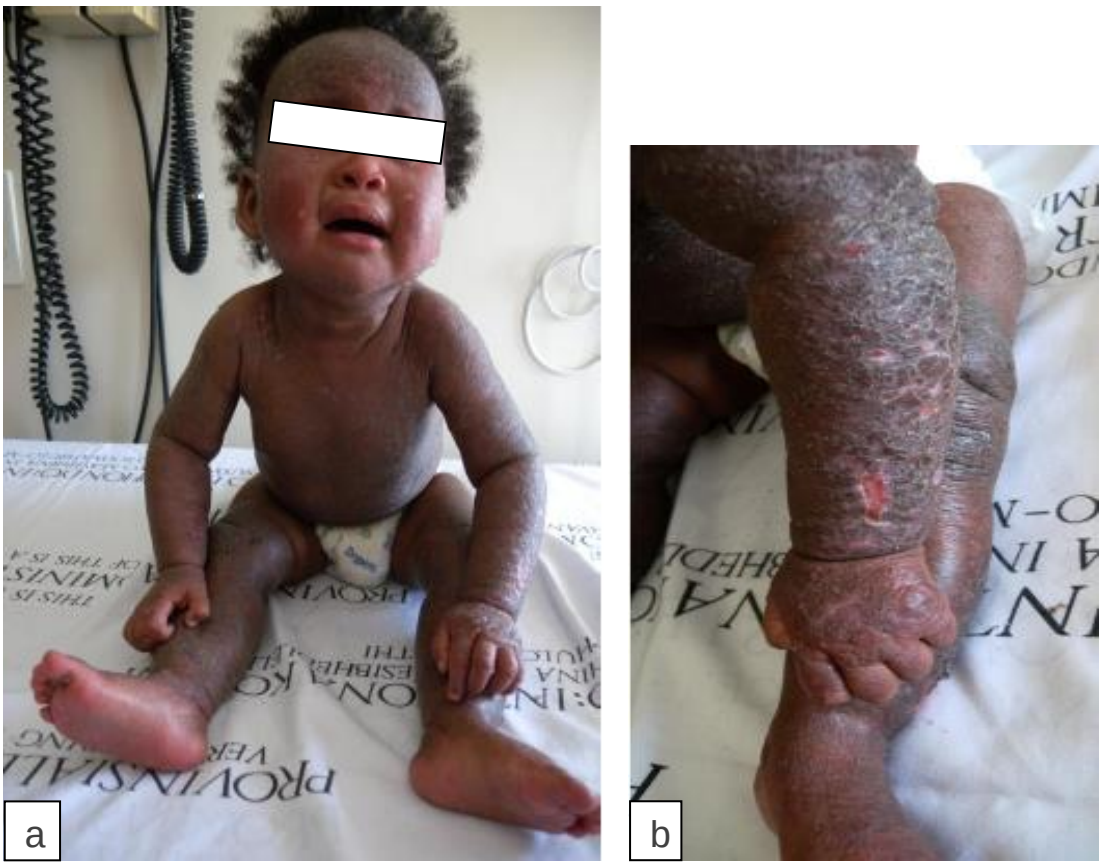

Figure 69 a and b: a)Severe atopic eczema presenting with extensive disease (erythroderma), and lichenification and excoriations. b) Close up shot highlighting the lesion on the limbs.

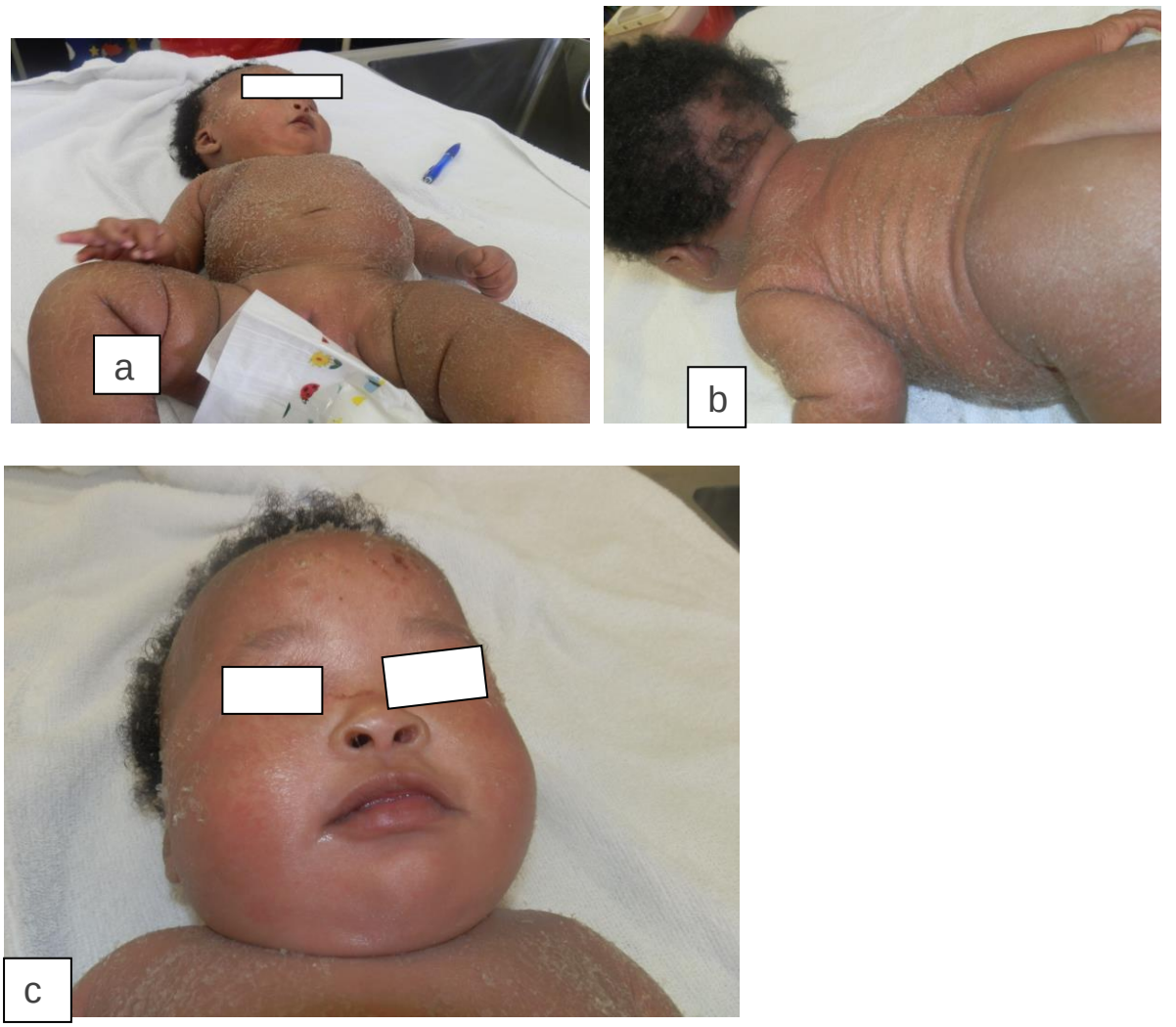

Figure 70a and b: Atopic dermatitis – Erythrodermic but less severe with mild scaling exfoliative dermatitis. c. Focus on face and upper chest wall. Note that the centre is face is spared in keeping with typical feature of atopic dermatitis.

Diaper Dermatitis (Contact Irritant Napkin Dermatitis)

Diaper dermatitis (DD) is the most common dermatitis found in infancy. DD was found to be one of the clinical markers of HIV infection in infants in an endemic area. Diaper dermatitis occurs when skin is exposed to prolonged wetness resulting in breakdown of the stratum corneum, the outer protective layer of the skin. Prolonged contact with urine and faeces is associated with irritant diaper dermatitis. Faecal proteases and lipases are the major irritants.

DD causes discomfort and predisposes infants to secondary infection including *Candida albicans*. It has also been found to be one of the clinical markers of HIV infection in infants in an endemic area.

Irritant contact diaper dermatitis is characterized by patches of erythema and scaling, mainly on the convex surfaces of buttocks, thighs, lower portion of abdomen, pubic region, labia majora, and scrotum

Diagnosis: Diagnosis of primary irritant diaper dermatitis is clinical. Mycological analysis to determine the contamination by Candida is indicated when there is intense erythema, satellite pustules or slow resolution of the disease.

Prevention: The key element of care in irritant contact diaper dermatitis is prevention. Frequent diaper changes are also important in preventing diaper dermatitis.

Treatment: Medical treatment of primary irritant diaper dermatitis consists of simple measures applied according to the severity and type of dermatitis.

Barrier creams made of zinc oxide, titanium dioxide and starch or creams with dexpanthenol may be used to avoid excessive humidity in the diaper area, minimize transepidermal loss of water and reduce skin permeability. These products may help prevent the contact of faeces with the already damaged skin, because they get adhered to the epidermis and are not easily removed with water.

Topical corticosteroids such as hydrocortisone may be applied if erythema persists. If dermatitis does not improve or there is marked erythema and pustules, Candida infection should be suspected and topical antifungals like clotrimazole commenced.

Further reading

1. Visscher MO. Recent advances in diaper dermatitis: etiology and treatment. Pediatr Health 2009; 3: 81-98.
2. Fernandes JD, Machado MC, Oliveira ZN. Clinical presentation and treatment of diaper dermatitis--part II.An Bras Dermatol. 2009; 84:47-54.
3. Jaspan HB, Myer L, Madhi SA et al. Utility of clinical parameters to identify HIV infection in infants below ten weeks of age in South Africa: a prospective cohort study. BMC Pediatr. 2011;11:104.

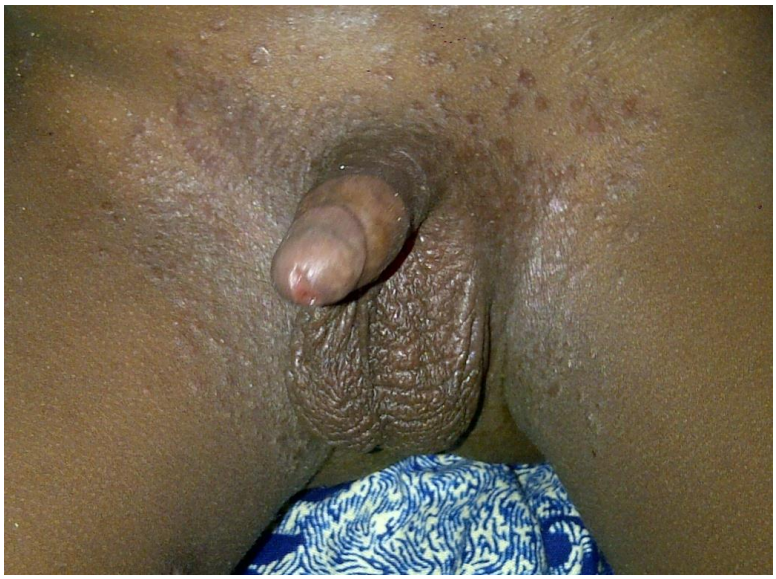

Figure 71: Diaper dermatitis in a dark-skinned child. (Courtesy: Dr Adewale Owa – University College Hospital, Ibadan)

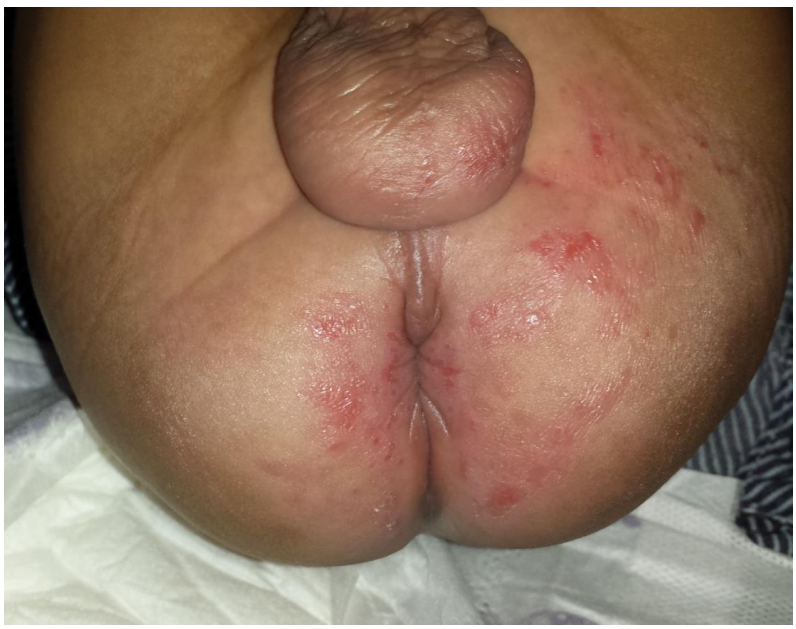

Figure 72: Diaper dermatitis

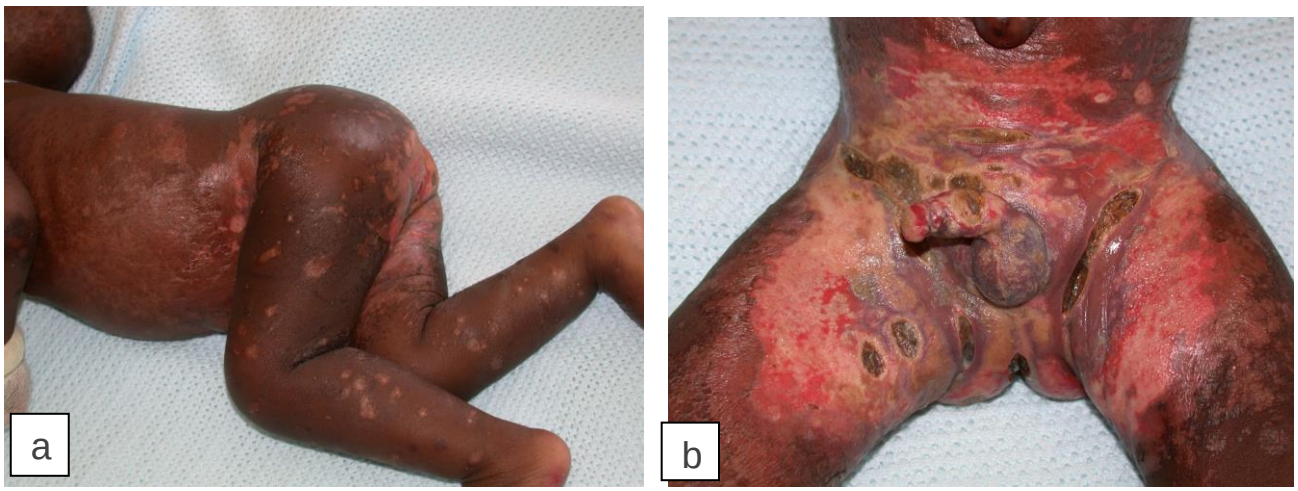

Figure 73: Necrotic ulcers of ecthyma complicating diaper dermatitis.

Psoriasis

Definition: Psoriasis is a chronic inflammatory skin disease characterized by excessively rapid keratinocyte proliferation.

Epidemiology: The prevalence of psoriasis in HIV-infected persons is the same as in the general population, however the disease is more severe in HIV-infected persons with falling CD4 counts.

Aetiology: Psoriasis has a strong genetic predisposition. In HIV, it is postulated that the immune dysregulation in advanced disease favors development of psoriasis.

Clinical features: **P**soriasis in HIV-infected persons has unusual presentations. It is severe and is associated with frequent exacerbations. Several morphological types often coexist in the same patient. The common presentations include plaque, erythrodermic, inverse psoriasis and reactive arthritis-like psoriasis syndrome.

Treatment: Treatment is generally challenging. Initiation of antiretroviral therapy and avoidance of triggers like smoking, beta-blockers and lithium improves response. Topical steroids, vitamin-D derivatives, coal tar and dithranol can be used in mild disease. Acitretin and phototherapy, if available, are recommended in moderate to severe disease. If these fail, under careful supervision, immunosuppressants like methotrexate and cyclosporine may be used.

Further reading

1. Morar N, Willis-Owen SA, Maurer T, Bunker CB. Lancet Infect Dis. 2010;10(7):470-8 HIV-associated psoriasis: pathogenesis, clinical features, and management.
2. Utikal J, Beck E, Dippel E, Klemke CD, Goerdt S. Reiter's syndrome-like pattern in AIDS-associated psoriasiform dermatitis. J Eur Acad Dermatol Venereol. 2003; 17(1):114-6.

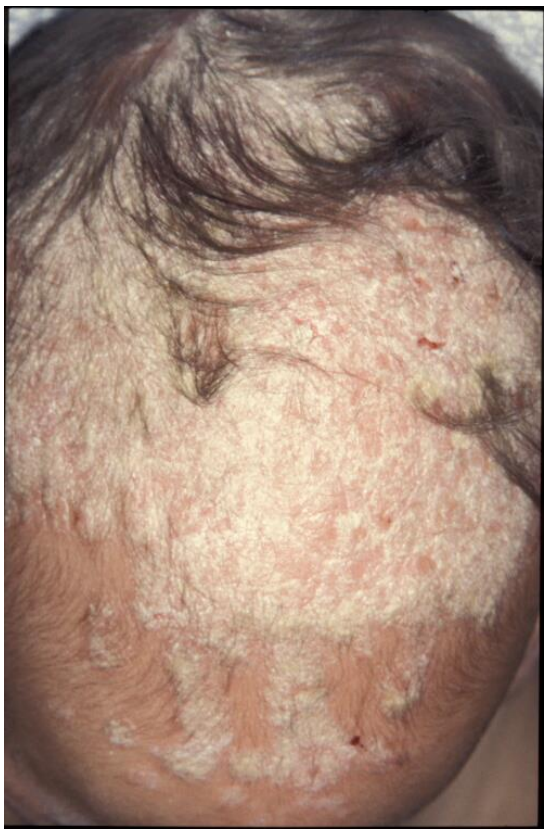

Figure 74: Scaly plaques of psoriasis on the scalp extending to the forehead.

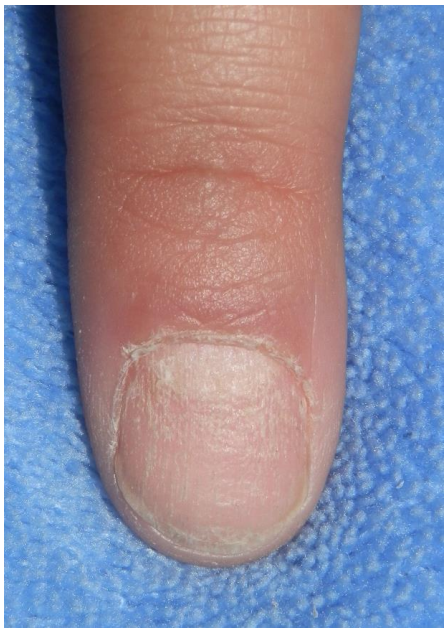

Figure 75: Pitting and longitudinal ridges on the finger nail of a child with psoriasis.

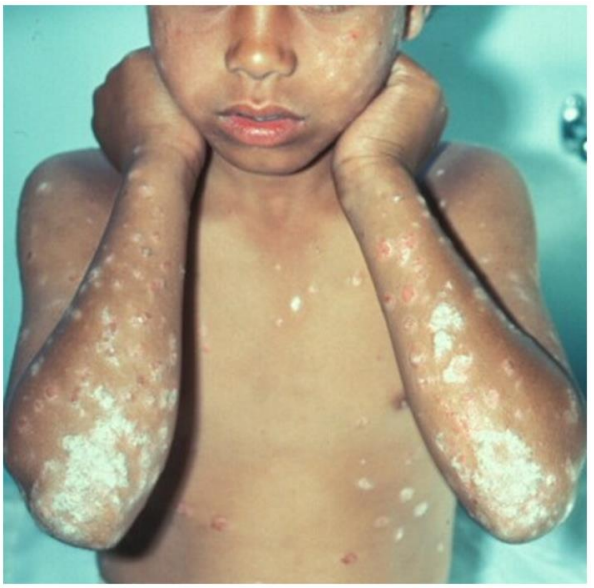

Figure 76: Silvery scales accentuated in the flexor surfaces of a child with psoriasis.

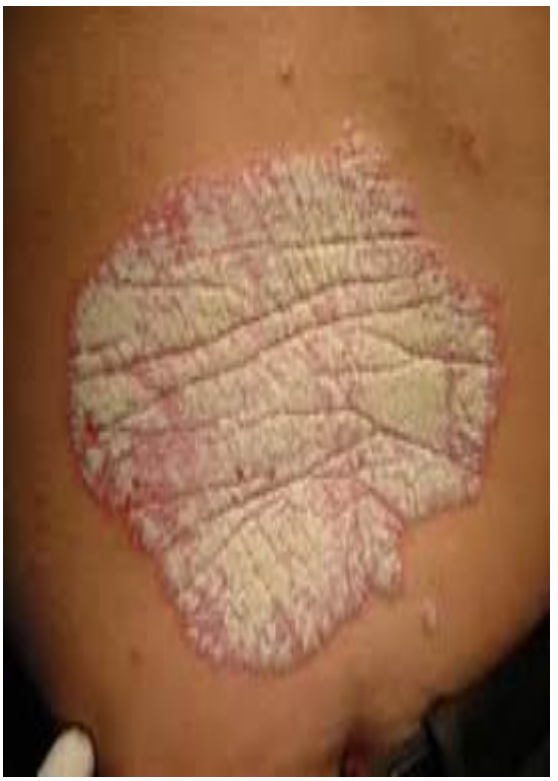

Figure 77: Thick scaly plaque of psoriasis on an erythematous background.

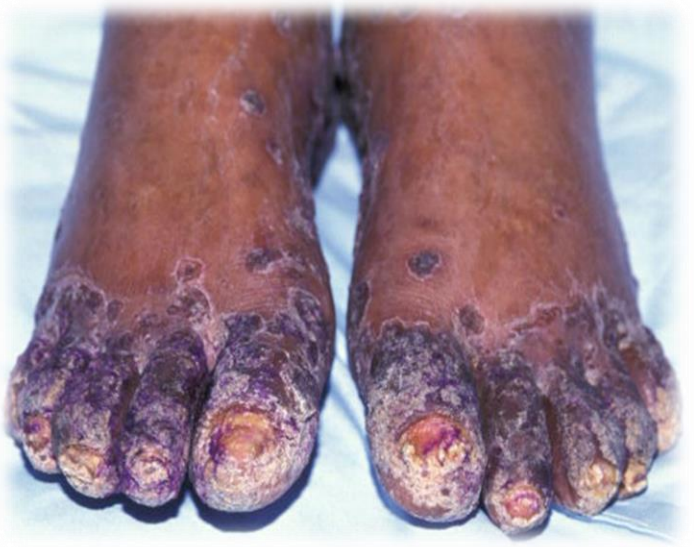

Figure 78: Hyperkeratotic psoriasis with severe nail dystrophy in HIV.

Pityriasis Rosea

Introduction: Pityriasis rosea is an acute, self-limiting disease, probably infective in origin, affecting mainly children and young adults, and characterized by a distinctive skin eruption and minimal constitutional symptoms.

Clinical features: Prodromal symptoms are usually absent. The first manifestation of the disease is usually the appearance of the herald patch, which is larger and more conspicuous than the lesions of the later eruption and is usually situated on the thigh or upper arm, the trunk or the neck; rarely it may be on the face, scalp or the penis. It is a sharply defined, erythematous, round or oval plaque, soon covered by fine scale.

The eruption consists of discrete oval lesions, dull pink in colour and covered by fine, dry, silvery-grey scales. The centre tends to clear and assumes a wrinkled, atrophic appearance and a tawny colour, with a marginal collarette of scale attached peripherally, with the free edge of the scale internally. The long axes of the lesions characteristically follow the lines of cleavage parallel to the ribs in a Christmas-tree pattern on the upper chest and back. The skin lesions commonly fade after 3–6 weeks, but some clear in 1 or 2 weeks and a few persist for as long as 3 months.

Treatment: Most cases require no treatment. Symptomatic treatment with antihistamines and topical steroids is often required and in severe cases UVB has sometimes been used. Oral erythromycin and high-dose acyclovir (20mg/kg) five times daily for 1 week), used early after the onset of the eruption, may lead to a more rapid clearance of skin lesions.

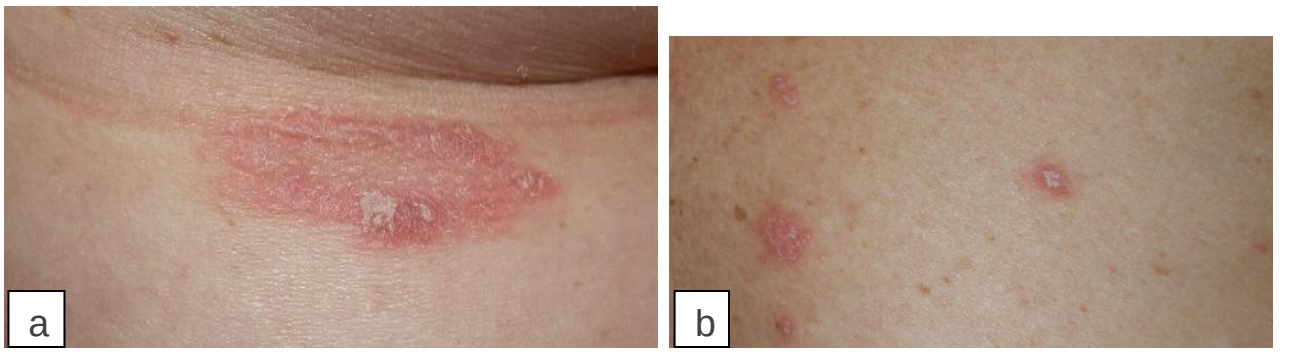

Figure 79a and b: (a) herald patch in a patient with pityriasis rosea. Note the later lesions in (b).

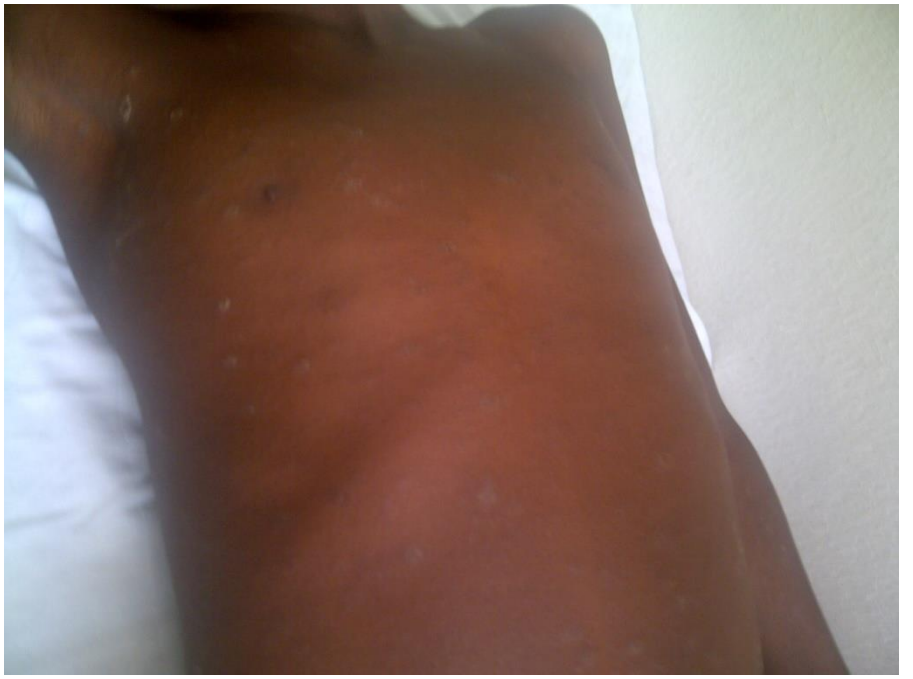

Figure 80: Pityriasis rosea- pigmented scaly plaques on the trunk.

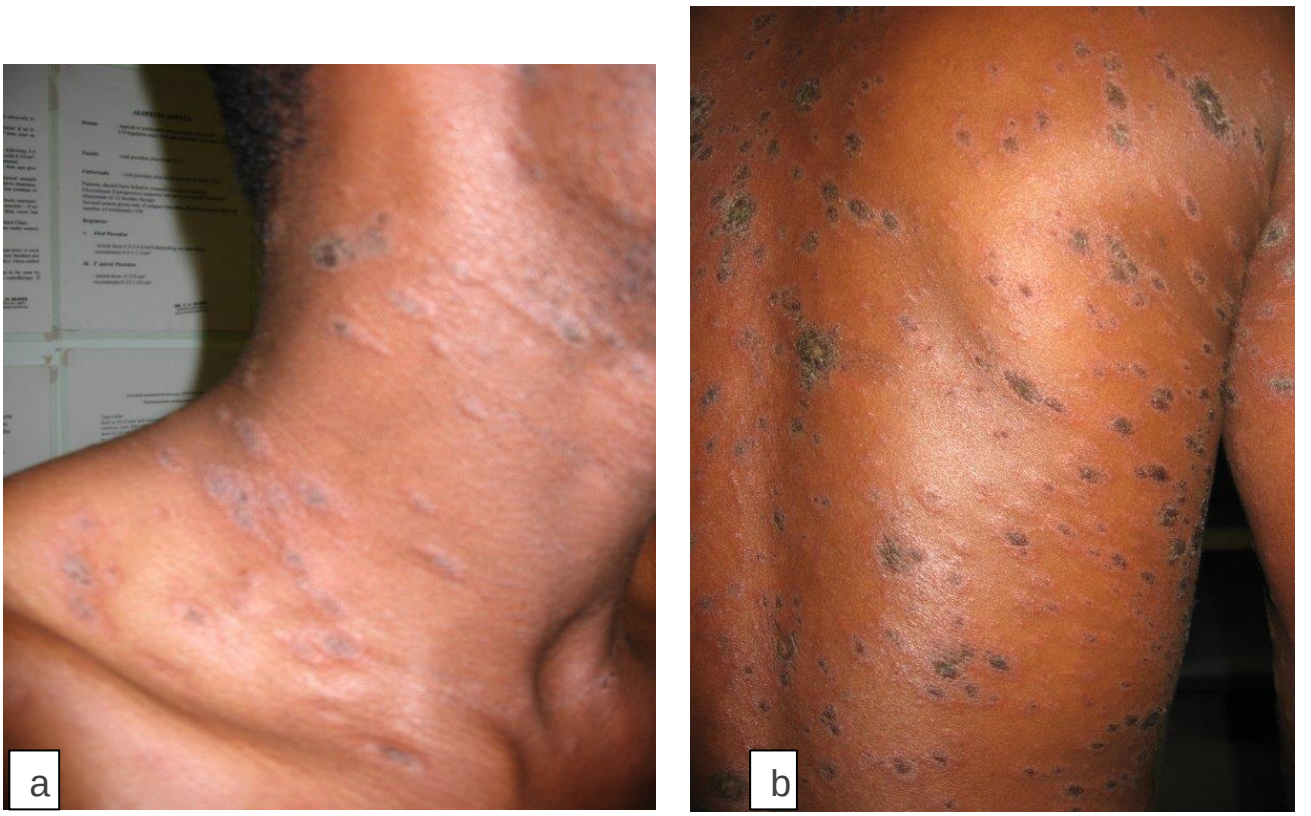

Figure 81a and b: Pityriasis rosea in an adult.

Xerosis

Description: This is the dryness of skin and a common cause of pruritus in HIV-infected persons.

Aetiology: Changes in cutaneous micro-circulation and nutrient supply to the skin.

Clinical presentation: dryness of skin, pruritus, excoriations.

Epidemiology: One of the most common non-infectious skin diagnoses in HIV-infected individuals. It is mainly seen in the extremities.

Prevention: Affected individuals should avoid soap and excessive washing.

Treatment: Skin hydration such as soaking in tub (using tepid or lukewarm water) followed by application of emollient. Mid-potency steroids (ointment is better than cream, since it contains lubricant).

Complications: Secondary bacterial infections.

Further reading

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3. Maurer TA. Dermatologic Manifestations of HIV Infection. International AIDS Society 2006; 13 (5): 149-154.
4. Singh F, Rudikoff D. HIV-associated pruritus: etiology and management. Am J Clin Dermatol 2003; 4 (3): 177-188.

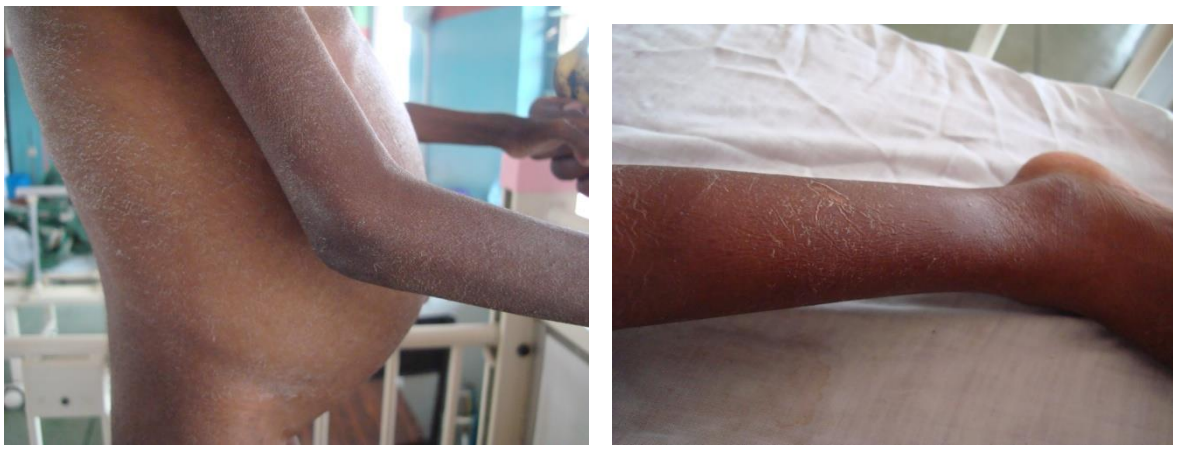

Figure 82 Xerosis in an HIV-infected child. Note the fine scale:

Acquired Ichthyosis

Description: The term ichthyosis is derived from Greek word ‘ichthys’, meaning fish and is basically a heterogeneous group of cutaneous keratinization disorders.

Aetiology: Can be congenital or acquired. Acquired Ichthyosis can be secondary to HIV, sarcoidosis, hypothyroidism and as a paraneoplastic phenomenon. In HIV, it is thought to result from wasting syndrome.

Clinical presentation: There are symmetrical large scales of the skin.

Epidemiology: Acquired Ichthyosis is among the most frequently encountered dermatologic disorders found in HIV-infected persons with advanced disease.

Diagnosis: Xerosis is a clinical diagnosis.

Prevention: Affected individuals should avoid soap

Treatment: ART, skin hydration and lubrication.

Further reading

1. Okulicz JF, Schwartz RA. Hereditary and acquired ichthyosis vulgaris. Int J Dermatol 2003; 42: 95–98.
2. Tlacuilo-Parra JA, Guevara-Gutie´rrez E, Salazar-Pa´ramo M. Acquired ichthyosis associated with systemic lupus erythematosus. Lu pus (2004) 13, 270 -273.

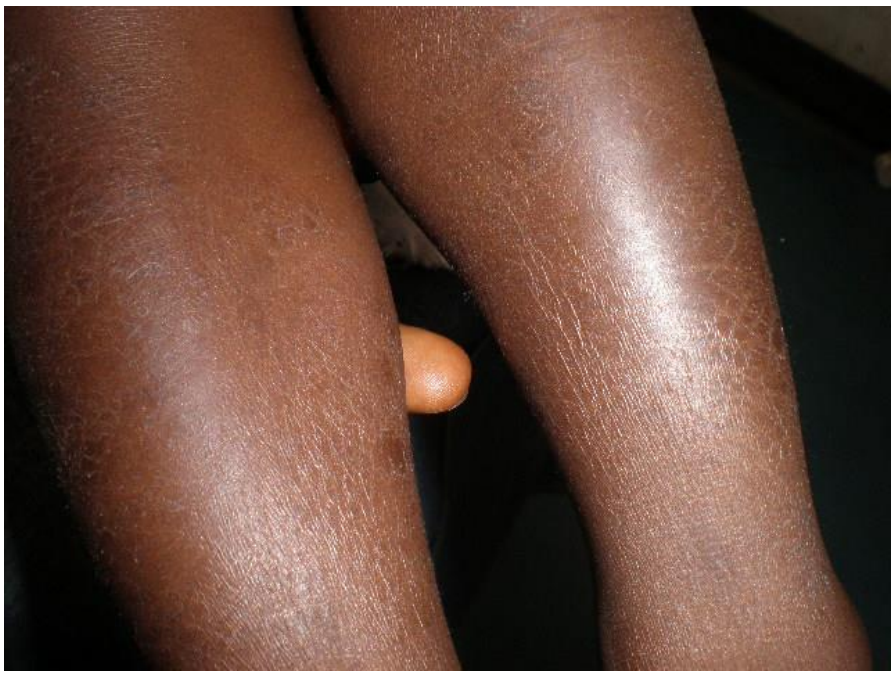

Figure 83: Ichthyosis on the shins - Note the crazy paving (fish scale) pattern.

CHAPTER 6: DRUG ERUPTIONS

Introduction: Drug eruptions are more common in HIV-infected individuals, up to 100-fold by some estimates - Mild and transient to life threatening, skin deep or multisystem. The reason for the increased incidence of drug eruptions in HIV-infected individuals may be as a result of the use of multiple medications including treatment for opportunistic infections and antiretroviral therapy; genetic predisposition; and HIV-associated immune dysregulation, which lowers the threshold of T cell activation coupled with persistent stimulation of CD8 T cells.

Classification

Two types of reactions to medications and they are either predictable (type A) and unpredictable (type B).

Type A includes lipodystrophy and pigmentation. Type B reactions include morbilliform eruptions, Steven Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN), drug rash with eosinophilia and systemic symptoms (DRESS) syndrome, erythroderma, vasculitis and fixed drug eruptions, lichenoid reactions.

Further reading

1. Luther J, Glesby MJ. Dermatologic adverse effects of antiretroviral therapy: recognition and management. Am J Clin Dermatol. 2007; 8(4):221-33.
2. Introcaso CE, Hines JM, Kovarik CL. Cutaneous toxicities of antiretroviral therapy for HIV: part I. Lipodystrophy syndrome, nucleoside reverse transcriptase inhibitors, and protease inhibitors. J Am Acad Dermatol. 2010 ;63(4):549-61; doi: 10.1016/j.jaad.2010.01.061.
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4. Sharma A, Vora R, Modi M et al. Adverse effects of antiretroviral treatment. Indian J Dermatol Venereol Leprol 2008; 74:234-7.

Table 5: Cutaneous reactions due to antiretroviral agents including both types A and B reactions

Antiretroviral drug	**Cutaneous reaction**
Nucleoside reverse transcriptase inhibitor (NRTI)	
Zidovudine	Mucocutaneous and nail hyperpigmentation, rarely: Hypertrichosis, vasculitis, paronychia
Stavudine	Lipodystrophy
Didanosine	Vasculitis, SJS, alopecia
Abacavir	Hypersensitivity reaction -Maculopapular eruption, urticaria, erythema multiforme
Lamivudine	Paronychia, allergic contact dermatitis
Non-nucleoside reverse transcriptase inhibitor (NNRTI)	
Nevirapine	DRESS, SJS
Efavirenz	Skin eruption (usually mild)
Etravirine	Maculopapular eruption (mild to moderate)
Protease inhibitors (PI)	
General	Lipodystrophy, hypersensitivity reaction
Indinavir	Paronychia, porphyria, SJS, alopecia, gynaecomastia
Nelfinavir	Maculopapular eruption, urticaria
Atazanavir	Maculopapular eruption, asymptomatic jaundice and sclera icterus
Darunavir	Maculopapular eruption
Integrase inhibitor	
Raltigravir	Diaphoresis

Type A reactions

Antiretroviral Lipodystrophy

Lipodystrophy syndrome (includes lipoatrophy and lipohypertrophy) is one of the long-term toxicities of stavudine (d4T) which was one of the back bones of first line antiretroviral therapy. Protease inhibitors (PIs) are also implicated in causing this syndrome.

Lipoatrophy is characterized by loss of subcutaneous tissue from facial pads, extremities, and buttocks. Apart from abnormal fat redistribution in stavudine toxicity, metabolic abnormalities including hyperlipidaemia may also be associated. Studies have reported a prevalence of between 18% and 33%. Stavudine is thought to cause lipoatrophy by inducing adipocyte apoptosis.

As a result of lipodystrophy and other toxicity effects of stavudine, national treatment programmes have dropped d4T and moved to zidovudine or abacavir based regimens. Replacing stavudine with abacavir or zidovudine resulted in improvement in established stavudine-induced lipoatrophy in HIV-infected subjects.

Further reading

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4. McComsey GA, Ward DJ, Hessenthaler SM et al. Improvement in Lipoatrophy Associated with Highly Active Antiretroviral Therapy in HIV-infected Patients Switched from Stavudine to Abacavir or Zidovudine: The Results of the TARHEEL Study. Clin Infect Dis 2004; 38:263-270.
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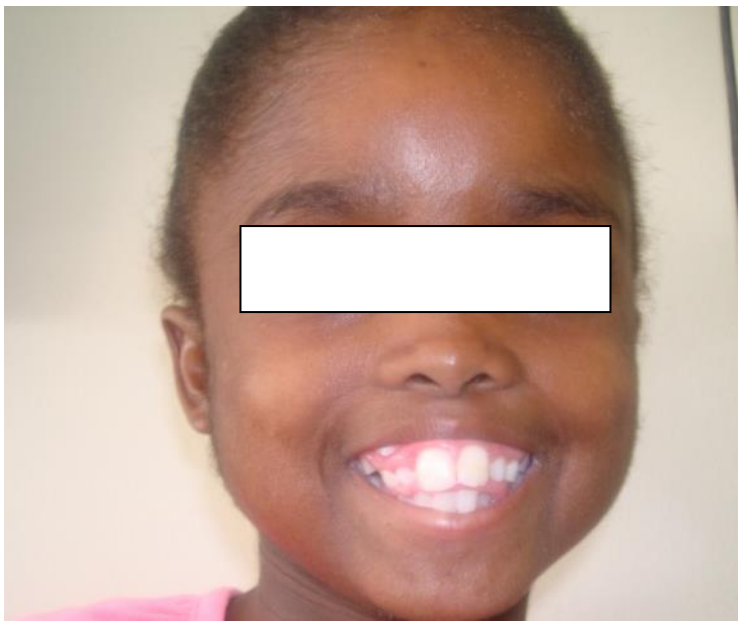

Figure 84 Nine year old girl who had been on stavudine based regimen from the first year of life. Stavudine was substituted with abacavir 6 months prior on account of lipoatrophy.

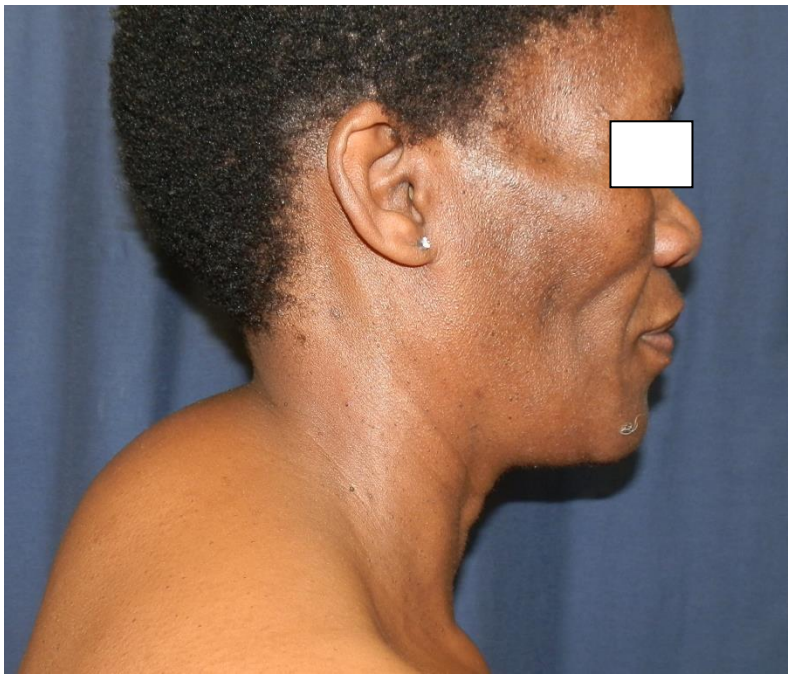

Figure 85: An adult with stavudine-associated lipodystrophy. Note the temporal wasting loss of buccal fat pad and the enlarged dorsocervical fat pad.

Type B reactions

Morbilliform drug eruptions

Definition and clinical presentation: Morbilliform (measles-like) drug eruption or maculopapular exanthems usually manifest 7–14 days after drug exposure. The lesions can progress and become confluent resulting in erythroderma. There are no associated systemic features. The rash is transient and treatment should not be interrupted. However, morbilliform rash can be the initial presentation of more serious reactions such as DRESS.

Aetiology: There is a very wide spectrum of drugs that cause morbilliform eruptions.

Epidemiology: This accounts for 95% of all cutaneous drug reactions.

Treatment: Usually not necessary, but topical steroids may speed up resolution.

Further reading

1. Bigby M. Rates of cutaneous reactions to drugs. Arch. Dermatol. 2001;137 (6): 765–770.

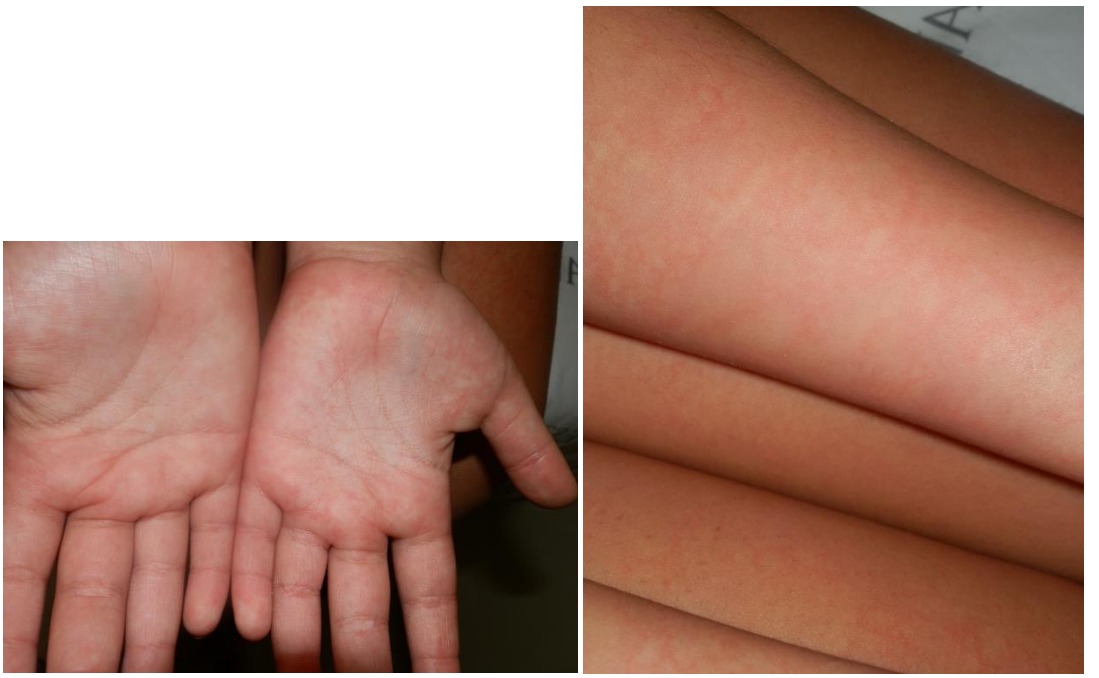

Figure 86: Transient morbilliform drug eruption on a young girl.

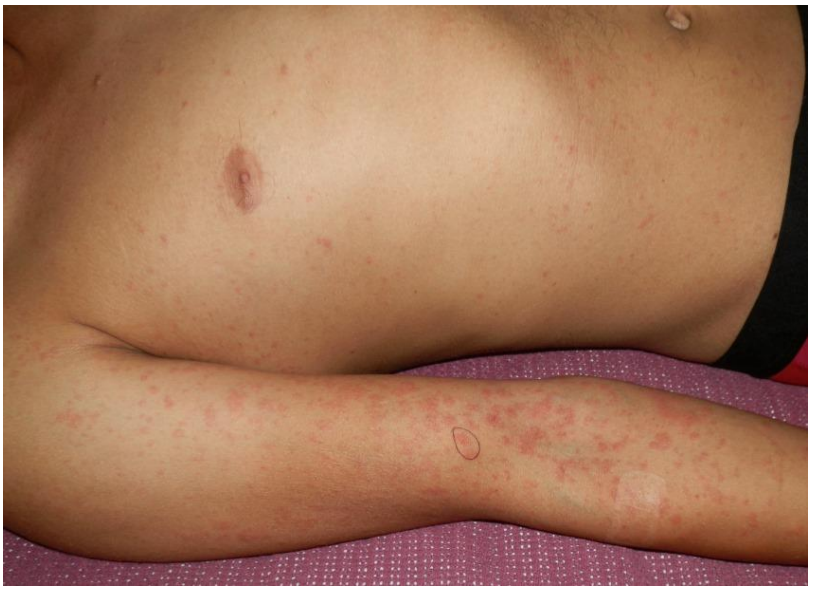

Figure 87: Morbilliform rash (measles-like) in an adolescent with a drug reaction.

Drug Rash with Eosinophilia and Systemic Symptoms (DRESS)

Definition and presentation: Also known as drug hypersensitivity syndrome is a drug reaction characterized by a long latency period (> 3 weeks), a rash, fever, oedema, lymphadenopathy, leukocyte abnormalities (leucocytosis, eosinophilia and/or atypical lymphocytosis) and hepatitis. The eruption is usually urticaria-like or maculopapular, but may present as vesicles, pustules or purpura.

Aetiology: A large number of drugs are associated with DRESS; however, in HIV-infected persons anti-tuberculosis drugs, co-trimoxazole and nevirapine are often implicated.

Epidemiology: **The incidence in HIV-infected people is much higher**

Treatment: Immediate withdrawal of the offending drug improves outcomes but treatment is mainly supportive. Topical steroids are helpful but in severe cases systemic steroids are used.

Complications: DRESS has mortality of up to 10%. Complications include liver failure, renal failure, myocarditis, pneumonitis and pancreatitis.

Further reading

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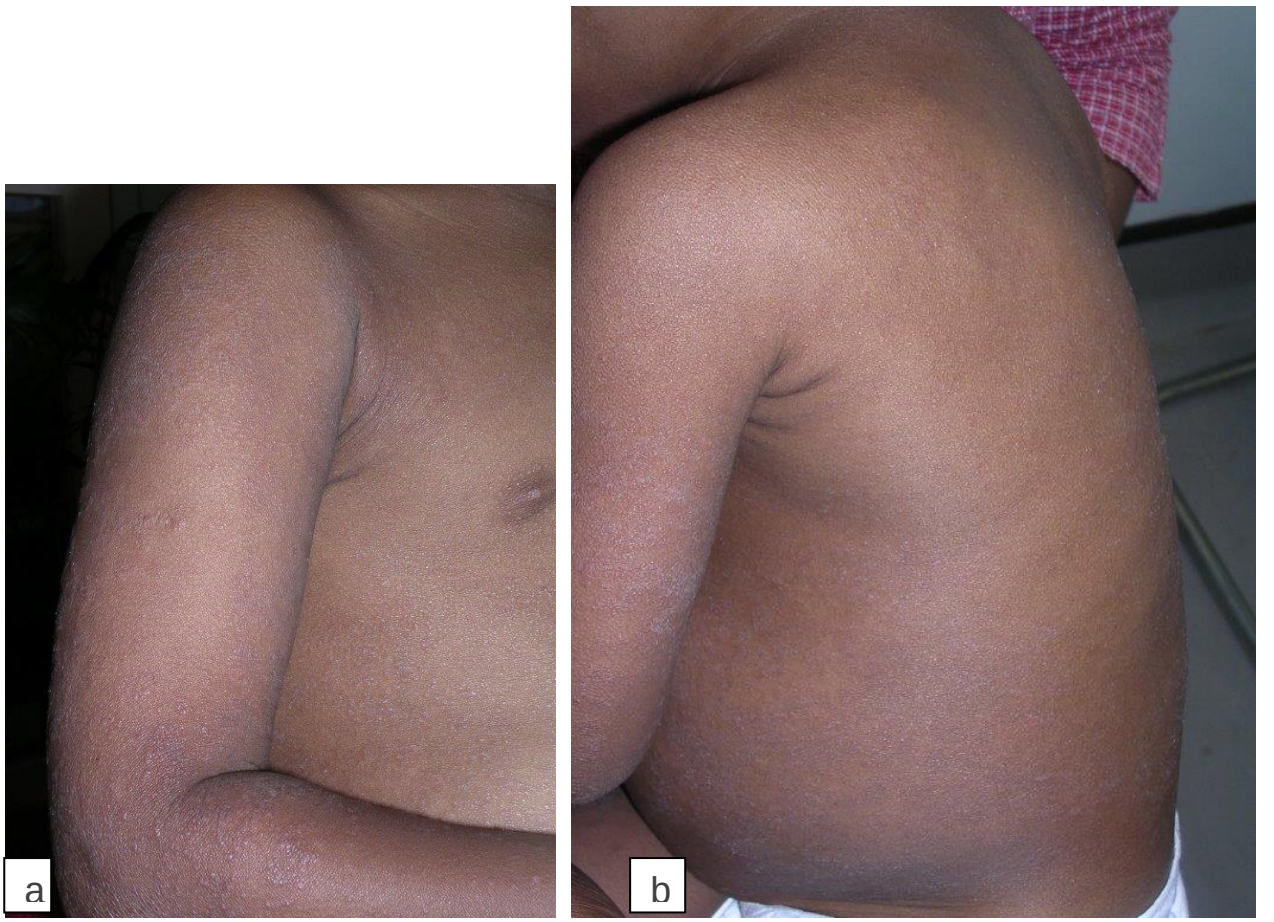

Figure 88a and b: DRESS

Abacavir Hypersensitivity

Abacavir (ABC) is a nucleoside analogue reverse transcriptase inhibitor. Approximately 3-5% of individuals who receive abacavir develop an immune-mediated hypersensitivity reaction (HSR) which occurs within the first six weeks of therapy. The HSR is rare but life threatening and is associated with individuals who carry the *57:01 variant in the human leukocyte antigen B (HLA-B) gene.

Diagnosis: The most common symptoms are fever, skin rash, gastrointestinal disorders and respiratory symptoms. A reduction in the incidence of abacavir hypersensitivity and unwarranted interruptions of therapy have been demonstrated with prospective screening for HLA-B*57:01 allele.

Considering the lower risk for abacavir hypersensitivity reaction and cost implications, implementation of genetic testing in this regard, in African settings in routine clinical practice may not be feasible. The importance of clinical monitoring of patients on abacavir cannot be overemphasized.

Treatment: Clinical management of suspected hypersensitivity reaction is discontinuation of abacavir and supportive care with analgesics, antihistamines, adequate fluids and appropriate laboratory monitoring for systemic organ involvement. Rechallenge with abacavir is contraindicated due to the risk of precipitating a life-threatening reaction.

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Nevirapine Hypersensitivity

Nevirapine (NVP) induced rash or toxicity occur in estimated 7-15% of patients receiving the drug. NVP rash can vary from a mild morbilliform rash to Stevens-Johnson syndrome. The rash typically develops within six weeks of initiating therapy. The introduction of NVP at a low dose with escalation over a 2-week period is recommended.

Patients with higher CD4 cell counts, including patients using NVP as post-exposure prophylaxis, are reported to have a higher risk of systemic hypersensitivity reaction, and therefore NVP is not recommended as part of post-exposure prophylaxis regimens.

A patient on NVP who develops a rash should be assessed for hepatotoxicity. If a morbilliform exanthem occurs in the setting of a fever, hepatitis, or other systemic symptoms, NVP must be discontinued immediately.

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Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)

SJS and TEN represent a spectrum of rare but potentially fatal mucocutaneous diseases characterized by widespread epidermal necrosis and mucosal involvement. SJS and TEN are considered to be part of a spectrum of severe cutaneous adverse reactions with increasing severity and extent of skin detachment, ranging from SJS (less than 10% body surface area skin detachment, 1-5% mortality) to TEN (greater than 30% skin detachment, 25-35% mortality).

In HIV-infected patients, the most common antiretroviral drug implicated to cause SJS/TEN is nevirapine and less commonly protease inhibitors. Co-trimoxazole and antituberculosis drugs are also implicated. Re-exposure to the drug results in recurrence.

Diagnosis: The reaction develops around 7-14 days after initiation of the drug. The rash is preceded by a prodrome with constitutional symptoms of high fever, malaise, myalgia and arthralgia. This is often misdiagnosed as an upper respiratory infection and treated with drugs that are later incorrectly blamed as offenders. Mucocutaneous lesions develop abruptly as macules that progress to papules, vesicles, bullae or confluent erythema.

Although minor presentations may occur, significant involvement of oral, nasal, eye (acute conjunctivitis, eyelid oedema, and crusting to conjunctival membrane or pseudomembrane, corneal erosions, conjunctival fornix foreshortening, and corneal ulcers), vaginal, urethral, gastrointestinal, and lower respiratory tract mucous membranes may develop in the course of the illness.

Treatment: Treatment should involve a multi-disciplinary team in a high-level health facility. Identification and withdrawal of the suspected offending agent is important. Supportive care involves analgesia and maintenance of adequate fluid and electrolyte balance. Frequent ophthalmological assessment and antiseptic/antibiotic eye drops 2-hourly are advocated. Barrier nursing and infection control prevention measures are important.

The use of prophylactic broad-spectrum systemic antibiotics, intravenous immunoglobulin (IVIG) and steroids is controversial. Topical cleansing/antibacterial agents could include 0.5% silver nitrate solution on gauze or 10% chlorhexidine gluconate washes or saline washes or polymixin/bacitracin or 2% mupirocin.

For wound care, silver sulfadiazine needs to be avoided. Removal of necrotic epidermis is discouraged, as intact epidermis prevents bacterial inoculation onto the underlying viable dermis. Paraffin gauze or hydrogel dressings may be beneficial. Biological dressings may be required (xenografts, allografts, skin substitutes).

Complications: Acute complications are similar to those of extensive burns. The high morbidity and mortality associated with the condition occurs mainly from infection. Long-term sequelae of SJS/TEN include; recurrence, dyspigmentation, oesophogeal and genital tract stenosis, eye problems, genital fibrosis. Multidisciplinary care during the acute stage is necessary to prevent these complications.

Further reading

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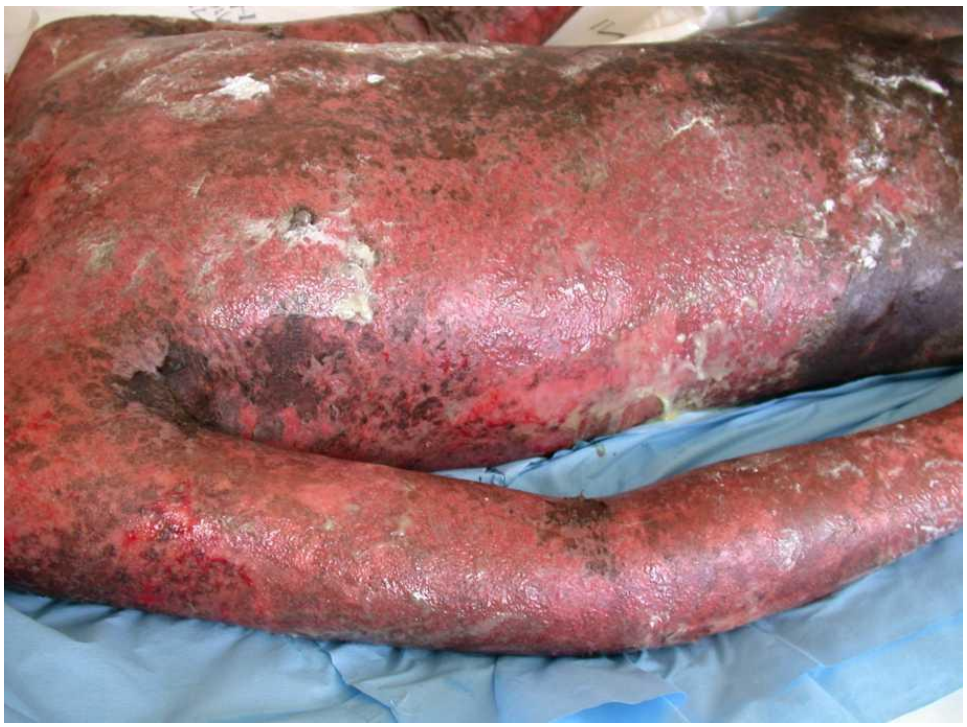

Figure 89: Extensive epidermal necrosis with areas of stripping in a case of TEN

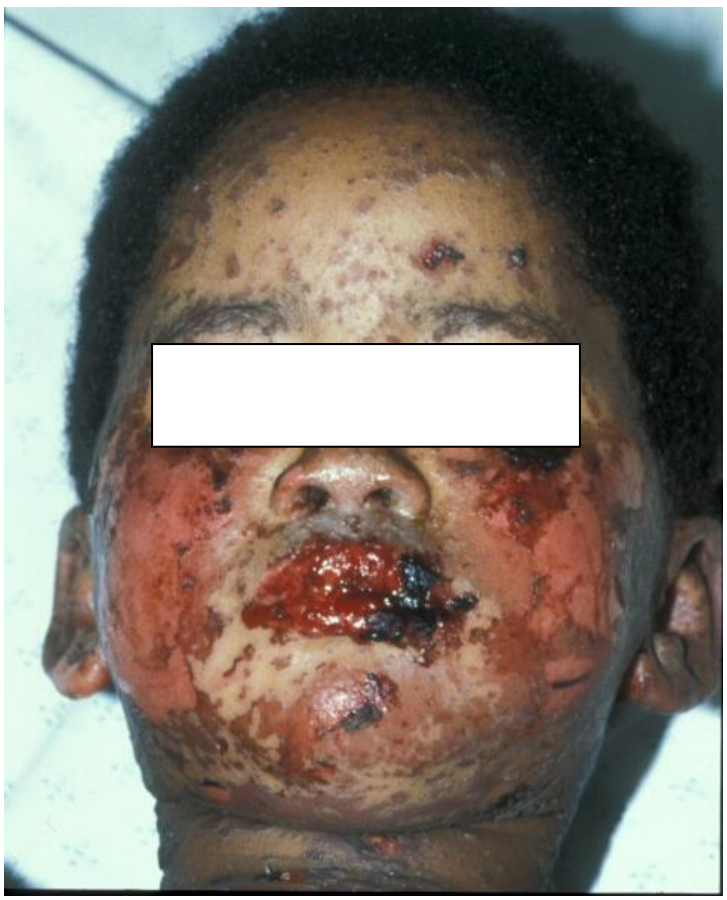

Figure 90: Epidermal necrosis with stripping and haemorrhagic cheilitis in a child with toxic epidermal necrosis.

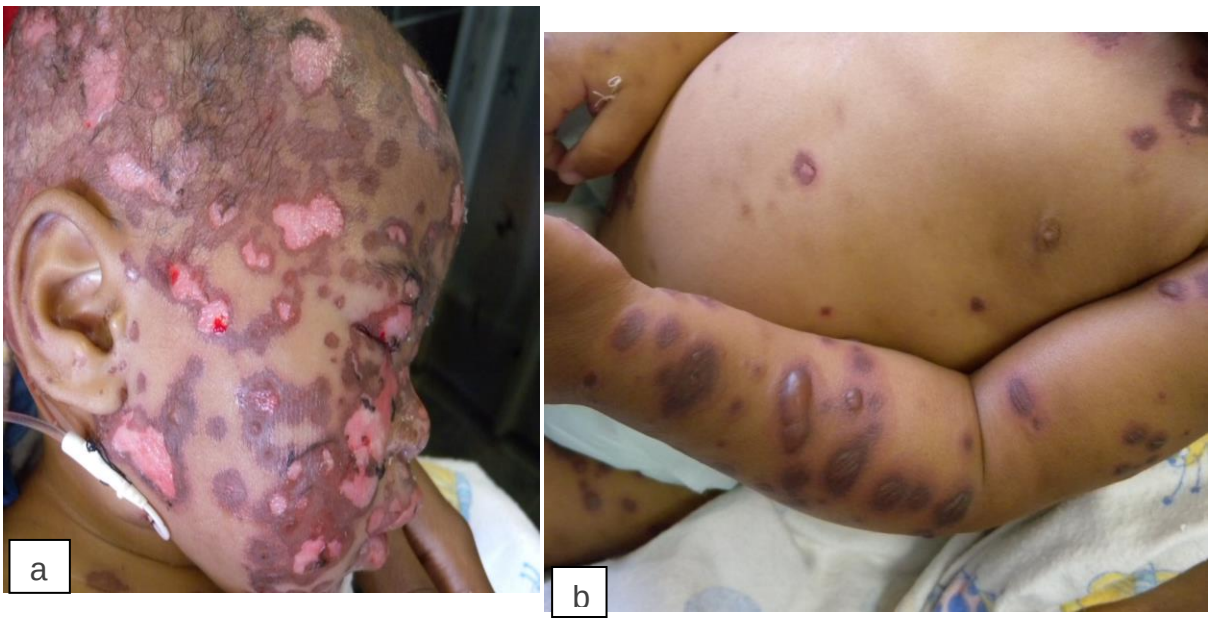

Figure 91a and b: Focal areas of epidermal necrosis with stripping in a case of SJS.

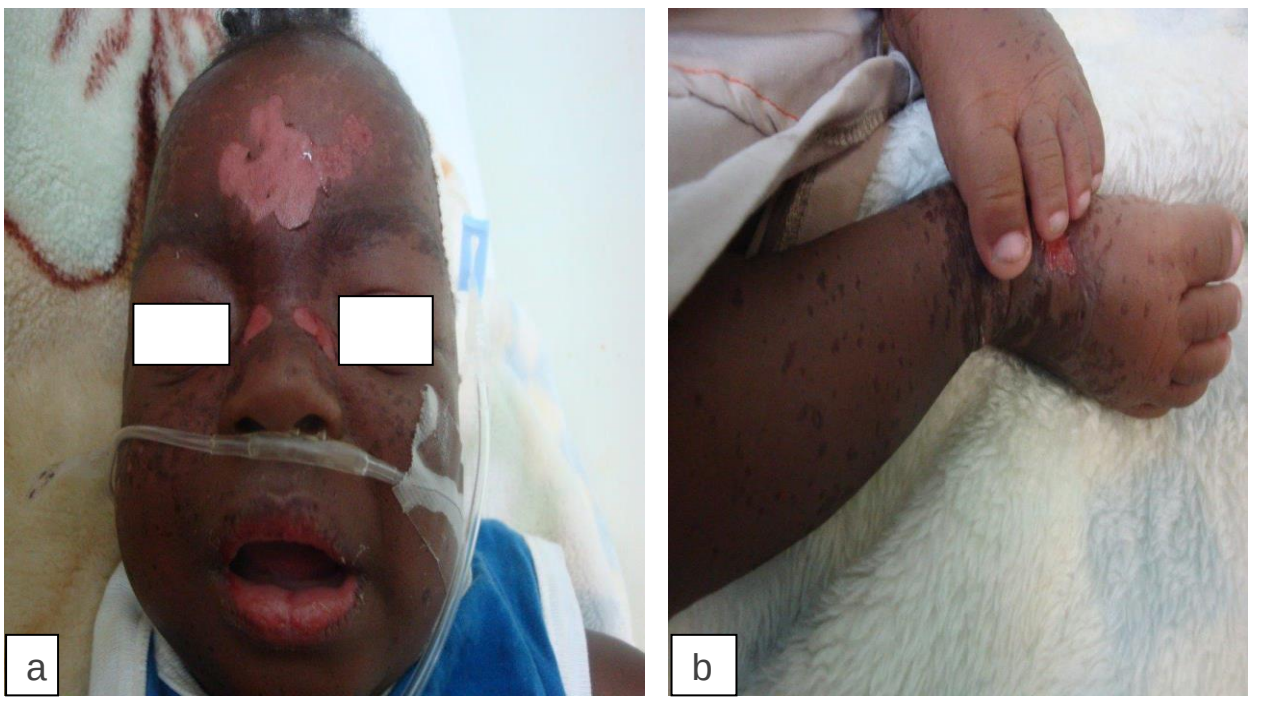

Figure 92a and b: SJS- Focal areas of epidermal necrosis with stripping.

Fixed Drug Eruptions

A fixed drug eruption characteristically recurs in the same site or sites each time the drug is administered. With each exposure, the number of involved sites may increase. Usually, just one drug is involved, although independent lesions from more than one drug have been described.

Cross-sensitivity to related drugs may occur, such as between tetracycline-type drugs, and between anticonvulsants. Fixed drug eruptions may occur with protease inhibitors. There may be a refractory period after the occurrence of a fixed eruption. Acute lesions usually develop 30 min to 8 hours after drug administration as sharply marginated, round or oval itchy plaques of erythema and oedema becoming dusky violaceous or brown, and sometimes vesicular or bullous.

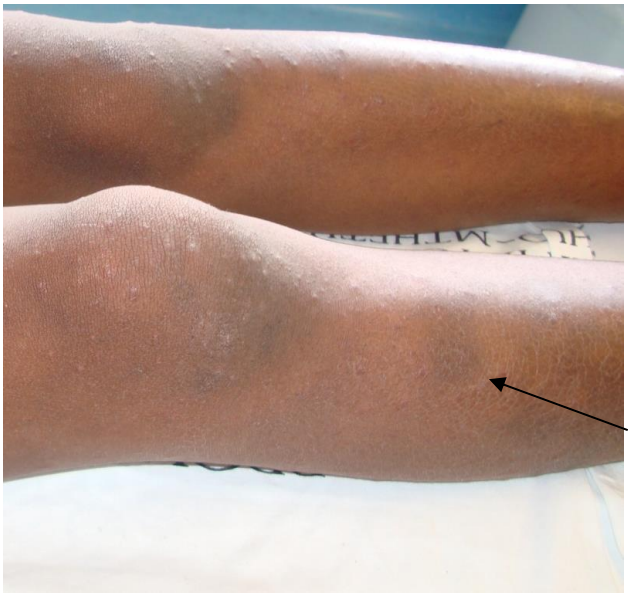

Figure 93: Mild fixed drug eruption/hyperpigmentation following cotrimoxazole prophylaxis therapy.

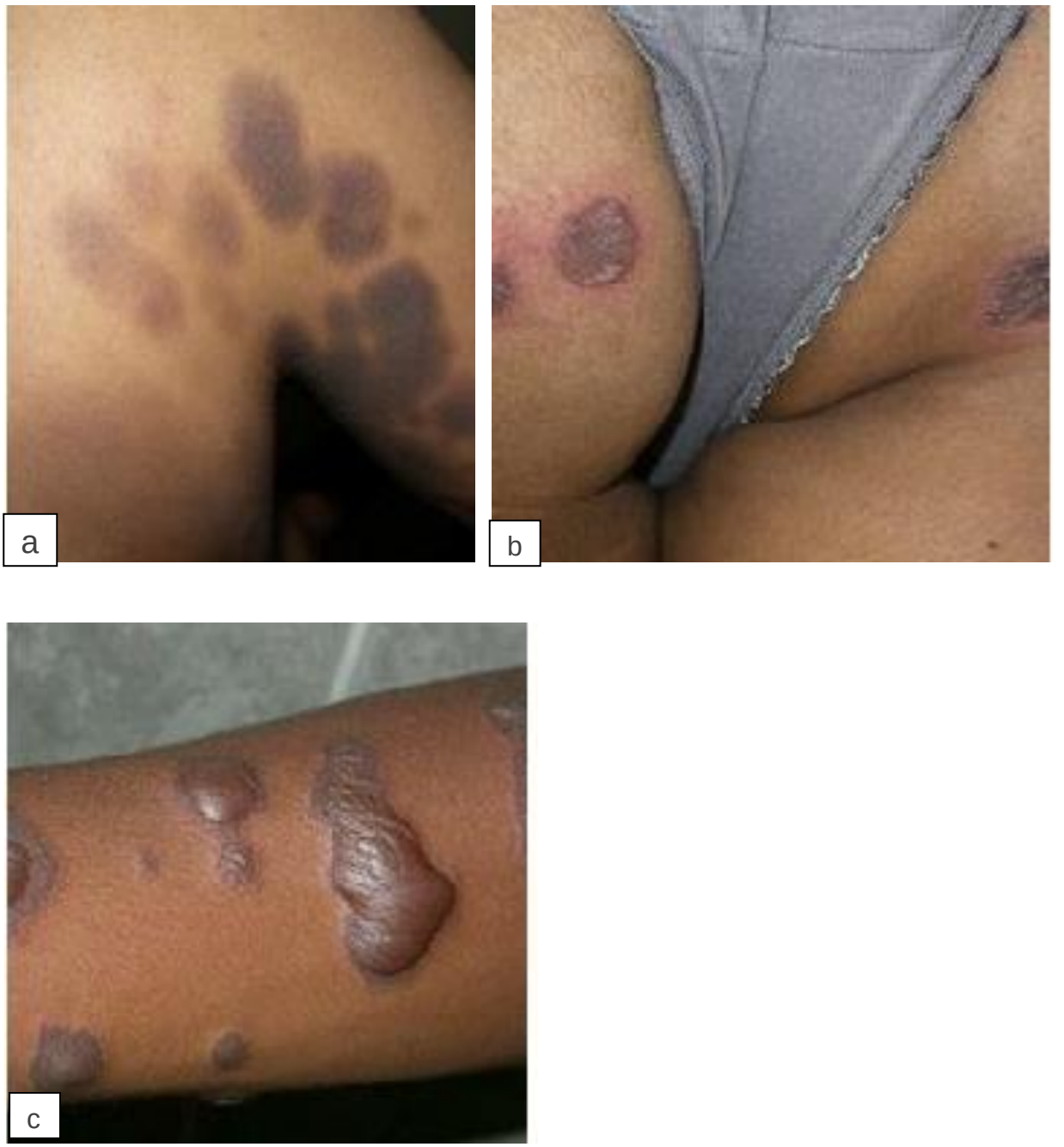

Figure 94a and b: Fixed drug eruption. a. Early lesions with rim of erythema and small blister. b. Bullous fixed drug eruption. c. Classic round pigmented macules of resolved fixed drug eruption.

CHAPTER 7: SKIN MANIFESTATIONS OF IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS)

Immune reconstitution syndrome (IRIS) is an inflammatory condition that may occur when HIV patients are started on antiretroviral medications. The cutaneous side effects of ART need to be differentiated from skin manifestations of IRIS. The restoration of immunity by effective ART in HIV-infected patients can cause temporary worsening of several infections and inflammatory skin disorders.

IRIS typically occurs in patients with low CD4 counts within the first 8 weeks of therapy (range – less than 1 week to several months). The most common types of infections seen as part of IRIS are ones that frequently affect the skin, including human papillomavirus in the form of genital, flat, or common warts, reactivation of the varicella-zoster virus or cytomegalovirus, cutaneous mycobacterial infection, or molluscum contagiosum. Inflammatory skin disorders associated with IRIS include atopic dermatitis and eosinophilic folliculitis.

In the management of cutaneous IRIS, ART needs to be continued while antibiotics, antivirals and steroids are added as appropriate.

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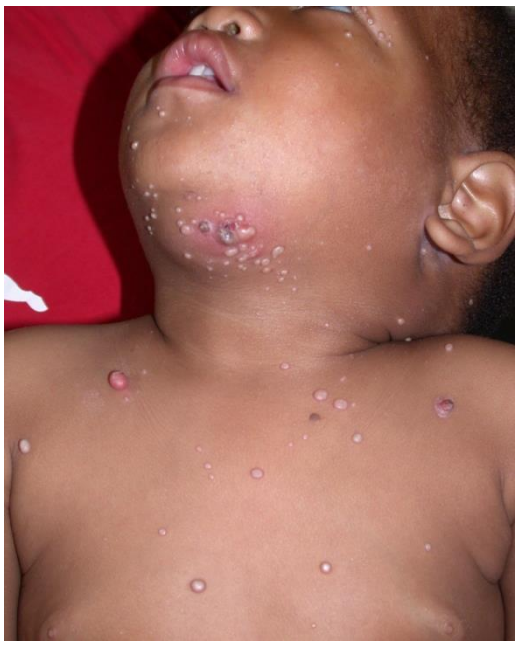

Figure 95: A flare-up of molluscum contagiosum following initiation of antiretroviral therapy.

CHAPTER 8: DISEASES OF SKIN APPENDAGES

Hair and HIV

Clinical presentations and epidemiology: Roughly 7% of HIV-infected persons present with telogen effluvium presenting as diffuse alopecia. The other findings include lengthening of the eyelashes, fine texture and straightening in late-stage disease. The hair also breaks more easily.

Aetiology and Treatment: The mechanism is thought to be multifactorial including nutritional deficiency, as a result of scalp inflammatory disorders like seborrheic dermatitis and autoimmune apoptosis of stem cells in the hair follicle. Alopecia, involving the scalp, has been reported in patients with HIV infection treated with indinavir and lopinavir/ritonavir. The alopecia will generally reverse after substituting the offending drug(s).

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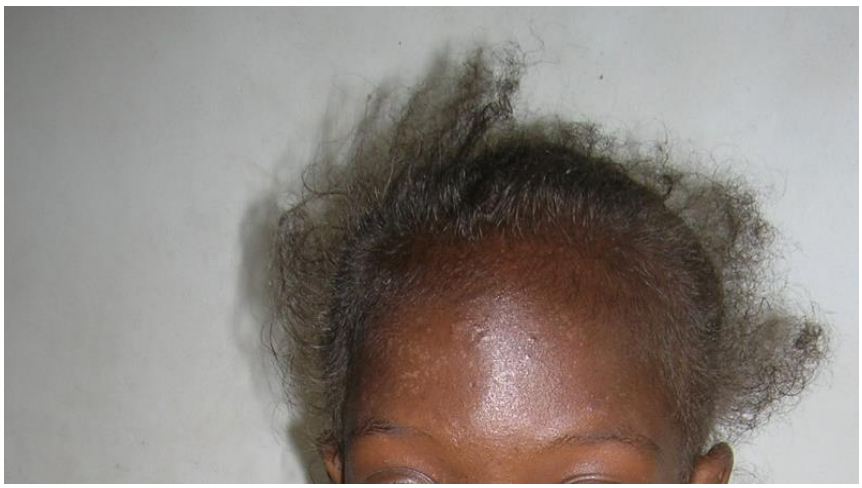

Figure 96: Hair changes in HIV infection.

Nail Changes in HIV

Nail abnormalities are reported twice as often in HIV-infected persons compared to the normal population.

The most common nail abnormality in HIV is onychomycosis occurring in a third of patients. It often presents with uncommon forms, namely proximal or superficial onychomycosis. There is often co-infection with mold fungi or candida.

Melanonychia is the darkening of the finger and toe nails. In HIV-infected individuals, it is characterized by longitudinal hyper pigmented lines in the nails. The increase in nail pigmentation is caused by amplified pigment production by melanocytes due to activation of nail matrix melanocytes. Longitudinal melanonychia associated may be associated with treatment by zidovudine.

Other features that are significantly more common in HIV include transverse ridging, clubbing, splinter hemorrhages, absence of lunula, periungual erythema and proximal or total leukonychia.

Treatment

Susceptibility to antifungal therapy is normal but onychomycosis in HIV-infected patients is more difficult to treat, probably as a result of co-infections. Thus, it is important to select a broad-spectrum antifungal therapy possibly for extended periods. There is no specific therapy for the other conditions except antiretroviral therapy.

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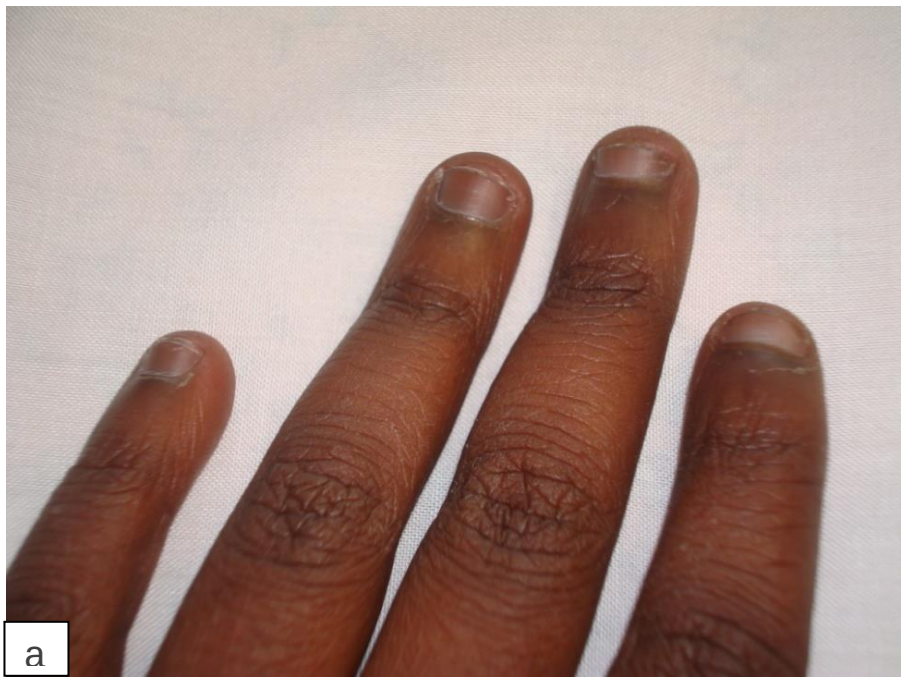

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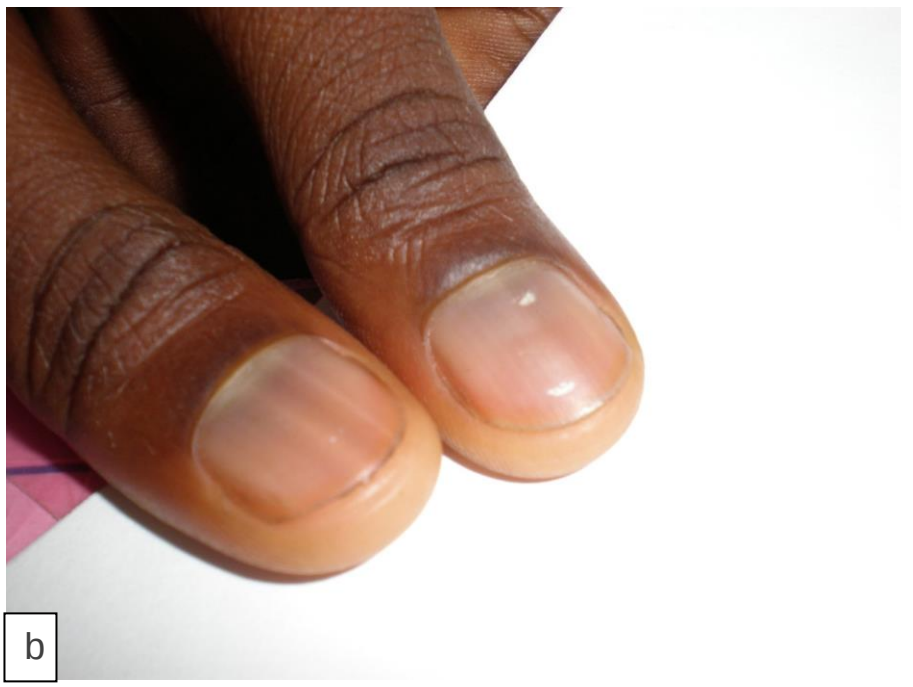

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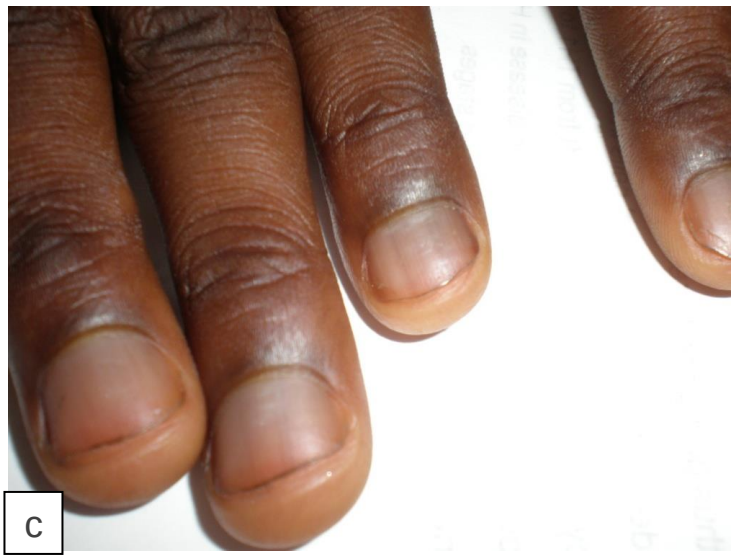

Figure 97a, b and c: Melanonychia

Digital Clubbing

Digital clubbing has been described in various pulmonary, cardiovascular, infectious, hepatobiliary and gastrointestinal diseases. It is characterized by bulbous enlargement of the distal phalanges due to an increase in soft tissue. Common causes of digital clubbing include cyanotic heart disease, neoplasms of the lungs, pulmonary tuberculosis, bronchiectasis, liver cirrhosis, and inflammatory bowel disease.

Its presence in concomitant HIV disease may be caused by lymphoid interstitial pneumonitis (LIP) or chronic lung disease.

Further reading

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