PREVALENCE OF CUTANEOUS MANIFESTATIONS IN HUMAN IMMUNODEFICIENCY VIRUS INFECTED CHILDREN AT KENYATTA NATIONAL HOSPITAL

A DISSERTATION IN PART FULFILLMENT FOR THE DEGREE OF MASTERS OF MEDICINE IN PAEDIATRICS AND CHILD HEALTH, UNIVERSITY OF NAIROBI

BY

DR. POLLY OKELLO (MBChB University of Nairobi),
DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH,
UNIVERSITY OF NAIROBI

2008

DECLARATION

This dissertation is my original work and has not, to my knowledge, been published or presented for a degree in any other university.

Signed ..... Date 02/10/08

DR POLLY OKELLO

We certify that this dissertation has been submitted for examination with our approval as university supervisors.

R. NDUATI, MBCHB, M.MED, MPH,

ASSOCIATE PROFESSOR OF PAEDIATRICS,

DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH,

UNIVERSITY OF NAIROBI.

Signature..... 25th September 2008

T.M. MUNYAO, MBCHB, M.MED,

SENIOR LECTURER, DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS,

UNIVERSITY OF NAIROBI.

Signature..... 2. October 2008

D.C. WAMALWA, MBCHB, M.MED,

LECTURER, DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH,

UNIVERSITY OF NAIROBI.

Signature..... 29th September 2008

DEDICATION

To God, who guides me in my endeavors

To my wife, for her unwavering support and encouragement

To my lovely daughters Ashley, Julie and Elsie – the angels in my life

To my parents and sister, an inspiration and example I cherish

ACKNOWLEDGEMENTS

I would like to express my sincere appreciation to my supervisors Prof R. Nduati, Dr T. Munyao, Dr D. Wamalwa for their encouragement, guidance, support and patience during the course of the study. A special thanks goes to Dr Munyao who spared his time to review the patients with me, Kipees and Lisa for their assistance in identifying the patients in the wards, Alice Lakati for her assistance in statistical analysis and finally, all the parents who accepted the participation of their children in the study.

TABLE OF CONTENTS

ABBREVIATIONS

AD	atopic dermatitis
AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
CCC	comprehensive care centre
CD	cluster of differentiation
CMV	cytomegalovirus
ELISA	enzyme linked immunosorbent assay
ESR	erythrocyte sedimentation rate
HAART	highly active antiretroviral therapy
HIV	human immunodeficiency virus
HPV	human papilloma virus
HZ	herpes zoster
IRS	immune reconstitution syndrome
KNH	Kenyatta National Hospital
KS	Kaposi's sarcoma
KOH	potassium hydroxide
MTCT	maternal to child transmission
NHL	non- Hodgkin's lymphoma
PCR	polymerase chain reaction
PGL	persistent generalized lymphadenopathy
PPE	pruritic papular eruption
SD	seborrheic dermatitis
SPSS	statistical package for social sciences
UON	University of Nairobi
SSSS	staphylococcal scalded skin syndrome
WHO	World Health Organization

LIST OF FIGURES **PAGE**

LIST OF TABLES

ABSTRACT

Objective: To compare the prevalence of various dermatological conditions between highly active antiretroviral therapy (HAART) - naïve human immunodeficiency virus (HIV) - infected children and HIV uninfected children at Kenyatta National Hospital (KNH).

Design: Cross-sectional study.

Methodology: HIV infected children were selected consecutively from the Comprehensive Care Centre (CCC) and the paediatric wards of KNH between September 2007 and February 2008. HIV uninfected children were also selected consecutively from the paediatric wards of KNH and matched for age with the HIV infected children. Patients were classified into four immune categories and a cluster of differentiation (CD) 4 cell count and CD4 percentage of total lymphocytes was performed on the HIV infected children. A medical history primarily focusing on skin symptoms and a complete physical examination was carried out on all the patients. Detailed examination of the skin from head to toe was undertaken. A clinical diagnosis of skin lesions was made by the principal investigator under the supervision of a consultant dermatologist. A digital camera was used to take photographs of the skin lesions. The history and physical examination findings, together with the results of all the investigations done on the day of the assessment, were recorded in the questionnaire/ record sheet. The data obtained was analyzed and conclusions and recommendations drawn from the results.

Results: The prevalence of skin conditions in HIV infected and HIV uninfected children was 37.0% (95% CI 27.5%-46.5%) and 21.0% (95% CI 13.0%-29.0%) respectively. Skin conditions were significantly more frequent (p=0.01) among HIV infected children. Prevalence of skin conditions in WHO stage 1, 2 and 3 was 20.0%, 27.5% and 57.6% respectively. Children with advanced HIV disease (WHO stage 3 and 4) had a significantly higher prevalence of skin disease (p=0.005) than those in stage 1 and 2. HIV infected children with a skin condition had significantly lower CD4 counts (p=0.003) and CD4% (p=0.001) than those without a skin condition.

Conclusions: Skin conditions were significantly more prevalent in HIV infected children as compared to HIV uninfected children. Skin conditions were significantly more prevalent in children with advanced HIV disease and lower CD4 count and percentage.

INTRODUCTION

Globally, the number of people living with HIV by end of 2005 has been estimated to be between 33.4 and 46.0 million. Amongst these, 2.3 million are children with more than 60% of them living in sub-Saharan Africa. The number of Kenyans living with HIV by the end of 2005 was 1.5 million of whom 150,000 were children.[1] In Kenya, the most affected are women in child-bearing age (15-49 years) with a potentially increased number of children with vertically transmitted HIV infection.[2] Over 90% of the infections in children are through mother to child transmission (MTCT).[3] Dermatoses are an important manifestation of HIV/AIDS and affect greater than 90% of patients at some stage of their illness.[4] Kaposi's sarcoma in young homosexual men was the first symptom that made AIDS a visible disease.[5] Since then more than 56 cutaneous disorders have been diagnosed in HIV-infected or AIDS patients.[6] This justified the inclusion of cutaneous manifestations of both HIV-infected adults and children in the Centers for Disease Control (CDC) classification.[7,8]

COMPARISON OF CLINICAL PRESENTATION OF COMMON SKIN CONDITIONS IN HIV INFECTED INDIVIDUALS AND HIV UNINFECTED INDIVIDUALS

As the search for reliable clinical indicators for management of HIV in resource-poor settings continues, cutaneous disorders of HIV should be considered among key clinical indicators of underlying immune status and disease progression.[9,10] It is observed that the incidence and severity of skin disorders increase as the immune function deteriorates. Nevertheless, data to substantiate this relation remains limited especially in resource poor settings.

Below is a brief description of some of the more common cutaneous manifestations in HIV albeit largely based on adult studies carried out in areas other than Africa since data in the paediatric population is deficient.

VIRAL INFECTIONS Herpetic infections of the skin and mucous membranes are frequent opportunistic infections in HIV-infected patients. The clinical symptoms differ substantially according to the patient's immune status. As long as the cell-mediated immune functions are normal, typical localized infections with itching, erythema and grouped vesicles will appear and heal spontaneously within a few days. In contrast, very painful, deep and large ulcerations of the anogenital region, face and other parts of the body appear in patients with advanced HIV infection and severe immunodeficiency. Varicella zoster virus (VZV) infections which are usually self-limited in immunocompetent children, can be very problematic for HIV-infected children. In children with AIDS, the interval between chicken pox (primary VZV infection) and shingles (reactivated VZV disease) may be reduced to weeks or months instead of decades.[11,12] Appearance of shingles in children and young adults serves as a clinical marker for HIV infection in high-risk groups and may be an indicator of progressive cellular immunodeficiency in HIV infected individuals.[13] HIV-infected children with low CD4 cell counts will typically exhibit extensive mucocutaneous disease with persistent new-vesicle formation.[11] The course of the disease in these patients can be chronic, progressive, and recurrent.

In HIV-infected patients, the clinical manifestations of molluscum contagiosum can differ significantly from those seen in the normal host. Spontaneous healing is rare and most patients have high numbers of lesions, typically occurring in the face and neck region, which is otherwise a rare location. The presence of multiple mollusca on the face is a typical disease marker, indicating advanced cell-mediated immunodeficiency. Immunodeficiency is associated with an increased incidence of Human papilloma virus (HPV) infection with more extensive disease and associated difficulty in therapy.[14] Some infants may acquire papillomaviruses

during passage through an infected birth canal, leading to recurrent respiratory papillomatosis. Genital warts appearing in childhood often results from sexual abuse.[15] Ulcers in the perineal region are the most common presentation for cytomegalovirus (CMV) infection in patients infected with HIV-1. The concurrent involvement of other infectious agents, such as HSV, in the same lesions confounds the role of CMV in cutaneous lesions. HSV is proposed to be the initiating infection leading to ulcer formation, with CMV secondarily localizing in the granulation tissue. A case of diaper dermatitis from cutaneous infection with cytomegalovirus was reported in a six month old boy with AIDS, who developed an intensely erythematous rash in the perineum with crusting, erosions, and bullae.[16]

PAPULOSQUAMOUS DISORDERS The prevalence of seborrheic dermatitis (SD) increases with HIV from 3% (in the general population) to between 34% [17] and 83%.[18] This trend is seen in women [19] and children [20] with HIV as well as in HIV-positive men. In Mali, where seborrheic dermatitis is quite rare, the development of this dermatosis in a patient has been used as a predictor for HIV infection.[21,22] Some authors also report that seborrheic dermatitis in HIV positive patients is more severe than usual [23] and that lesions of the extremities are more common.[24] These clinical observations have led to the suggestion that 'seborrheic-like dermatitis of acquired immunodeficiency syndrome' should actually be regarded as a distinctive entity [24] caused by immunologic defects. Psoriasis vulgaris may develop at any stage of HIV infection [25] and, as with SD; a rapid onset of eruptive psoriasis can serve as an important clue to underlying HIV infection. An inverse distribution involving inguinal creases and genitalia may be observed.[26] The psoriasis is often aggressive and may be associated with significant nail dystrophy, arthritis and Reiter's disease; it tends to worsen with declining immune status. Secondary bacterial infection with sepsis has been reported.[27] The prevalence of Pruritic papular eruption (PPE) in Africans and Haitians with HIV varies from 12% to 46%, depending on the geographic area.[28] Cases have been reported with similar frequencies in infected men, women, and children.[29] It is uncommon in immunocompetent patients. The typical

primary lesion is a firm, discrete, erythematous, urticarial papule. Persistent pruritus is usually refractory to topical steroids and oral antihistamines.[30]

NEOPLASIAS In 1981, Friedman-Kien et al. described more than 50 previously healthy, young homosexual men with Kaposi's sarcoma (KS) involving lymph nodes, viscera, and mucosa as well as skin.[5] This aggressive and frequently fatal epidemic variant of KS affected homosexual men with AIDS 20 times as frequently as it did male patients with hemophilia and AIDS who had similar degrees of immunosuppression.[31] Cutaneous AIDS-related B-cell non-Hodgkin lymphomas in HIV infection, appear earlier and more often on unexpected sites like the trunk and extremities. Cutaneous T-cell lymphomas are rare malignancies in HIV-infected patients. The prevalence among 2149 HIV patients in Frankfurt/M. was 0.06%. Biggar et al (2001) calculated a 15 fold higher relative risk for cutaneous T-cell lymphomas in HIV-infected patients in comparison to the general population.

FUNGAL INFECTIONS In the immunosuppressed population, superficial infection may not always result in pruritus or pain, and skin involvement may be very widespread. Dermatophyte infection is often refractory to treatment in these patient populations as well. [32] Most children with AIDS will develop oral candidiasis in the course of their illness.[33] Cutaneous candidiasis is even less commonly seen than the oral form in those with HIV infection. However, candidal intertrigo with characteristic satellite lesions has been described in immunosuppression.[34] Cryptococcosis is the most common invasive fungal infection in HIV-infected patients. Cutaneous cryptococcosis secondary to dissemination is considered an AIDS-defining illness. Skin manifestations of disseminated cryptococcosis occur in 10–20% of patients, and presentation is variable.[35] Cryptococcal skin manifestations in HIV-infected patients include molluscum-like lesions, cellulitis, erythematous papules, nodules, pustules, and oral ulcers.[36] Skin lesions occur in 10–20% of patients with disseminated histoplasmosis, as a result of hematogenous dissemination. Presentation is highly variable,

including nodules, papules, plaques, ulcers, vesicles, pustules, abscesses, and a general dermatitis.[37,38] Previously considered a relatively rare opportunistic infection, blastomycosis is an increasingly recognized infection in immunocompromised hosts.[39] The skin and subcutaneous tissue are the most common sites of extrapulmonary dissemination. Acute blastomycosis has only a 5% incidence of dermatologic symptoms. Skin involvement is characterized by small papules with central umbilication (with or without necrosis), similar to lesions seen with molluscum contagiosum. Lesions are usually encountered on the face, scalp, upper trunk, and upper extremities [40] and may resemble those resulting from *Histoplasma* and *Cryptococcus* infection; genital ulcers may also be present.[41]

BACTERIAL INFECTIONS Impetigo and folliculitis may be recurrent and persistent in HIV disease, particularly in children. Disseminated furunculosis and abscess formation can occur in patients with HIV infection. Skin lesions caused by *P aeruginosa* infection are more common in advanced stages of HIV infection and include ecthyma gangrenosum, erythematous macular or maculopapular lesions, and violaceous nodules.[42] Cellulitis may be caused by *S aureus*, group A streptococci, *Hemophilus influenzae* type B, group B streptococci, and *P aeruginosa*. Adenitis may be caused by typical bacterial pathogens, such as *S aureus* and group A streptococci, but also may involve bacteria such as *Streptococcus viridans*, *Enterobacter* spp, and *Staphylococcus epidermidis*.[43] Perirectal abscesses are seen more frequently in immunosuppressed patients, especially those with neutropenia. The most frequently isolated bacteria include *Bacteroides* spp, *P melaninogenicus*, *Peptostreptococcus* spp, *Escherichia coli*, *Klebsiella pneumoniae*, and *S aureus*. In addition, *Enterococcus* spp and *Acinetobacter* spp have been reported in HIV-infected children.[43]

MYCOBACTERIAL INFECTIONS *Mycobacterium tuberculosis, Mycobacterium avium-intracellulare* complex, and, rarely, *Mycobacterium kansasii* may present as acneiform papules and indurated crusted

plaques. The different patterns of cutaneous TB include scrofuloderma, lichen scrofulosorum, lupus vulgaris, TB verrucosa cutis, papulonecrotic tuberculid and erythema nodosum. Several studies have reviewed cutaneous TB in adults. Although there are a few series on the clinical expression of the disease in the paediatric age group, none has commented in detail on histopathological characteristics.[44]

OTHERS A number of reports suggest that the clinical spectrum of syphilis and the rapidity of disease progression may be modified by the presence of HIV.[45] Scabies is the most common ectoparasite infestation in HIV infected patients. In general, the clinical presentation does not differ from that seen in HIV-negative persons. Thrombocytopenic purpura, vitiligo, alopecia areata, sicca syndrome, pemphigoid, and other autoimmune blistering diseases have been reported in association with HIV disease. Atopic disease may be reactivated by HIV disease. Atopic eczema may be severe in children infected with HIV. Increased serum IgE levels have been found in these children; however, increased IgE levels were not correlated with atopic symptoms. Urticaria may occur primarily or as a drug eruption in HIV disease. Cutaneous vasculitis has been reported with HIV disease. Photosensitivity has been reported in patients with advanced HIV disease.

TABLE 1: COMPARISON OF COMMON SKIN DISORDERS IN HIV INFECTED AND UNINFECTED CHILDREN [46]

DISORDER	HIV-1 UNINFECTED CHILD	HIV-1 INFECTED CHILD
IMPETIGO	Discrete areas of erythema with honey-crusting, small blister formation	Lesions similar in appearance but may be extremely widespread or evolve into cellulites
ORAL THRUSH	Discrete white-yellow patches and plaques on tongue, palate, buccal mucosa; usual rapid response to topical therapy	Lesions may be more extensive, with involvement of entire oral cavity and posterior pharynx; poor response to topical therapy
MONILIAL DIAPER DERMATITIS	Confluent erythema with satellite pustules; responds to topical imidazole creams	Lesions may be more widespread; rapid recurrence after cessation of therapy
TINEA CAPITIS	Discrete areas of scale and hair loss; responds well to treatment	Areas of involvement may extend to face and recur after treatment
HERPES SIMPLEX	Primary herpetic gingivostomatitis is sometimes followed by recurrences of vermillion border of lip; lesions on other parts of face or on fingers may also occur.	Severe and persistent infection of oral mucosa, fingers or other skin surface may occur
HERPES ZOSTER	Relatively rare. Correlates with occurrence of chicken pox during infancy and childhood	Lesions tend to be more painful and result in scarring; may develop chronic varicella-zoster infection

DISORDER	HIV-1 UNINFECTED CHILD	HIV-1 INFECTED CHILD
WARTS	Single or multiple lesions on hands and other skin locations common	Lesions may be extremely widespread or persistent; extensive flat warts and giant condyloma acuminata may occur
SCABIES	Discrete, intensely pruritic papules or nodules in axilla, diaper area; rapid response to topical treatment	Widespread papular lesions or diffuse eczematous eruption; may recur after treatment
MOLLUSCUM CONTAGIOSUM	1-2 mm umbilicated papules on face, trunk, extremities	Lesions may be extremely widespread; giant lesions may occur
SEBORRHEIC DERMATITIS	Erythema covered with greasy looking scales over areas rich in sebaceous glands; scalp, face, chest, back and flexural areas.	More severe and lesions of the extremities are more common.

CUTANEOUS MANIFESTATIONS AS MARKERS OF HIV DISEASE PROGRESSION IN ADULTS

Few studies have been carried out to correlate mucocutaneous manifestations of HIV/AIDS infection with CD4 counts and disease progression. In a 2004 study in Nigeria, it was found that CD4 count of HIV positive patients with mucocutaneous manifestations was statistically correlated with low counts.[47] Seborrheic dermatitis occurred at CD4 counts of >200 cells/mm^3 as an early skin manifestation. Kaposi sarcoma and cryptococcus skin lesions occurred at CD4 counts of < 200 cell/mm^3 and < 50 cells/mm^3 respectively. A 2003-2004 Singapore study found that a CD4 count of < 200 cells/mm^3 was significantly associated with higher numbers of skin disorders and increased incidence of PPE, psoriasis and adverse drug reactions.[48] A similar study done in Thailand in the year 2000 found that patients with advanced HIV infection had significantly more skin disorders than those with early stage disease. The most common cutaneous manifestations in patients with CD4 counts of < 200 cells/mm^3 were xerosis and pruritic popular eruption while seborrheic dermatitis was prevalent in CD4 counts above 200 cells/mm^3.[49] A study carried out in Malaysia in 1997 concluded that patients with a CD4 count of < 50 cells/mm^3 had more severe skin manifestations. However, in this study the mean CD4 count for patients with seborrheic dermatitis was 34 cells/mm^3.[50] In a 2000-2001 India study, an inverse relationship was found the CD4 counts and the incidence of skin disease in the HIV/AIDS patients. Also, in comparison with the CD4 cell count of the aymptomatic HIV-positive individuals, the CD4 cell count of HIV-positive patients with dermatological manifestations was statistically correlated with low counts.[51] Infections were the most prevalent skin condition encountered (viral, bacterial and fungal, in order of decreasing prevalence).

CUTANEOUS MANIFESTATIONS AS MARKERS OF HIV DISEASE PROGRESSION IN CHILDREN

Children, unlike adults, have an immature immune system which is more deficient in the control of HIV infection.[52] Moreover, infants show higher viral load levels and also higher CD4+ T-cell counts than adults because they naturally have lymphocytosis at birth.[53] The result is a severe cellular immunodeficiency with a greater susceptibility to several infectious, inflammatory and malignant diseases. Thus, it is known that the humoral immunity is more severely affected in HIV-infected children than in adults, making them more prone to develop bacterial infections, particularly in the skin.[54] Skin manifestations have been shown to be a valuable clinical indicator of stages of HIV infection and associations have been established between some skin conditions and CD4 cell counts in HIV-infected individuals.[55] Although most studies of cutaneous disorders in HIV infected patients have been carried out in adults, mucocutaneous manifestations in HIV-infected children differ from those in adults in several respects, such as the lower incidence of characteristic lesions such as KS and oral hairy cell leucoplakia.[46]

Two Thai studies have been conducted in children relating mucocutaneous manifestations and degree of immunosuppression. These were carried out by Siriwan et al in 1996-1998 and a subsequent study in 1997-2000. In the earlier study, mucocutaneous manifestations were found in 51.6% of the children and were significantly more common in clinical categories B and C as compared to A. The most common findings were oral candidiasis, prutitic popular eruption, herpes zoster and cutaneous candidiasis.[56] In the latter study, the prevalence of mucocutaneous findings in children with severe, moderate, and no evidence of immunosuppression were 62%, 43% and 20% respectively. It was also found that mucocutaneous findings in patients in the moderate and severe suppression groups were significantly more common than in patients without evidence of immunosuppression.[57]

CUTANEOUS MANIFESTATIONS IN THE GENERAL PAEDIATRIC POPULATION

In a cross-sectional survey done in a primary school in Nigeria in 2005, prevalence of skin disease was found to be 35.2% with majority of the children having dermatophytosis (15.2%). Other commonly observed skin manifestations included scabies, pityriasis versicolor.[58] A prospective study done in Ethiopia in 1995-1997. Allergic skin diseases were most frequently found (55%) followed by infections(33%) and photodermatosis(8%). Of the allergic skin diseases atopic dermatitis was the most prevalent(47%) followed by seborrheic dermatitis(17.4%).[59] In a study done in 1999 by Popescu et al in Romanian primary school children, the prevalence of skin conditions was found be 21%.[60] In a study done in two primary schools in Turkey in 2002, infectious skin diseases were most frequently observed (pediculosis capitis, scabies and viral skin conditions).[61] In a study done in Hong Kong in 1997, the overall prevalence of skin conditions in children and adolescents in a student health service centre was 31%. Acne vulgaris and tinea cruris were distinctly more common in secondary school children while atopic eczema and congenital melanocytic nevi were more common in primary school children.[62]

No studies have previously been carried out to find out the prevalence of skin disease in HIV infected children in Africa. No study in Africa has correlated the presence of skin disease and clinical and immunological stages of HIV. Two Africa-based studies, both in Nigeria, were in the general paediatric population in two schools. No data is available from Africa on prevalence of skin disease in HIV infected children. The results in the Thailand studies have no comparative data from Africa. There may be differences in the cutaneous manifestations found in HIV infected children in our set-up as compared to the Thai children probably because of different environment or genetic profile. Our study aims to determine the prevalence of skin disorders in HIV infected children and correlate presence of skin disease with immunological status and clinical stage of HIV infection.

STUDY JUSTIFICATION

Cutaneous manifestations, which may be the initial signs of virus-related immunosuppression, frequently occur in HIV infected children. Recognising HIV-related skin changes may lead to the diagnosis of HIV infection in the early stages which provides early entry into comprehensive care including nutritional support, prophylaxis against common pathogens and subsequently antiretroviral therapy.

Dermatological manifestations of HIV may present differently due to differences in race, age, sex and environment. Skin lesions associated with HIV are well described in Western literature but there is no such description in Kenya. Few studies have been carried out in Africa on cutaneous manifestations of HIV infection in children.

STUDY OBJECTIVES

PRIMARY AIM

To compare the prevalence of skin disease between HAART- naïve HIV- infected children and HIV uninfected children at Kenyatta National Hospital.

SECONDARY AIMS

To correlate presence of skin disease among HAART naïve HIV-infected children with clinical stage.

To correlate presence of skin disease among HAART naïve HIV-infected children with immunological stage.

METHODOLOGY:

STUDY DESIGN

Cross sectional study

STUDY AREA

Patients were recruited from Comprehensive Care Centre (CCC) and Paediatric wards at the Kenyatta National Hospital (KNH). KNH is the only national referral hospital in Kenya. It is the teaching hospital for the University of Nairobi and serves as a provincial hospital for residents of Nairobi and its environs. CCC is located at KNH and was established in December 2003. Counselling is done at the CCC and ARV (antiretroviral) drugs are free to children who fulfil the entry criteria (depending on the WHO clinical stage, CD4 count and percentage and caregivers duly counselled on adherence). HAART was made available to children from 2005. The Centre for Disease Control (CDC) supports the AIDS Care and Treatment Services (ACTS) program through PEPFAR (Presidential Emergency Plan for AIDS Relief). ACTS program supports the data system, testing of children, including those who are HIV exposed.

STUDY POPULATION

HIV infected children drawn from paediatric wards and CCC, both located in KNH, and met the inclusion criteria.

INCLUSION CRITERIA

1. Children below 12 years of age with confirmed HIV infection either by rapid antibody tests in parallel, ELISA or PCR (cases).
2. HIV uninfected children matched for age (controls).
3. Informed consent from parent or legal guardian.

EXCLUSION CRITERIA

1. HIV positive children on HAART.
2. Severely malnourished children (Z score<3 SD).

SAMPLE SIZE DETERMINATION

The sample size was determined using the statistical formula for cross-sectional studies

$$N = \frac{[p_1(1-p_1) + p_2(1-p_2)]}{(p_1-p_2)^2} \times (Z_{\alpha/2} + Z\beta)^2$$

$Z\alpha = 2.56$

$Z\beta = 1.282$

$\alpha = 0.05$

$\beta = 0.10$

p1 = 0.51 [p1=prevalence of skin disease in HIV infected children. Siriwan Wanakul, Pakistan]

p2 = 0.21 [p2=prevalence of skin disease in HIV uninfected children. Popescu R, Romania]

Therefore the sample size = 68

Controls = 68

PROCEDURE

RECRUITMENT PROCESS

Children 12 years of age and below with confirmed HIV infection either by rapid antibody tests in parallel, ELISA or PCR and HIV uninfected children matched for age were recruited into the study after the parent or legal guardian had signed a written consent form following a detailed explanation of the purpose of the study. Patients who were severely malnourished or on HAART were excluded from the study. All consent forms were signed in duplicate. HIV infected and uninfected children were recruited by consecutive sampling until the required sample size was attained. HIV infected children were recruited from the paediatric wards and CCC while HIV uninfected children were recruited from the paediatric wards on the same day that the HIV infected children were recruited into the study.

CLINICAL ASSESSMENT

A medical history primarily focusing on skin symptoms was conducted. A complete physical examination was then carried out on recruited patients. Detailed examination of the skin from head to toe was carried out. A clinical diagnosis of skin lesions was made by the principal investigator (appendix IV). A consultant dermatologist reviewed all patients with skin lesions. A digital camera was used to take photographs of the skin lesions and these were archived as part of patient examination findings (appendix VIII). A detailed questionnaire was used to collect the necessary information on medical history and clinical findings (Appendix II).

SAMPLE COLLECTION

Provider initiated testing for HIV antibody and confirmatory PCR test for those aged < 18 months of age is offered to all children admitted to the paediatric wards of KNH. All children diagnosed to be HIV-infected from the wards had their CD4+ T-cell count and percentage done for immunological staging (appendix III) of the disease as part of pre-HAART preparation. Sample collection for immunological studies was taken at the Paediatric Department laboratory, University of Nairobi. Skin scrapings, where indicated, were taken for KOH (see appendix VI). Other samples included skin biopsy, pus swab and aspirate. Both procedures were done by the principal investigator.

QUALITY CONTROL

The principal investigator attended Paediatric dermatology clinic for several weeks before starting the study to gain some skills in diagnosing different skin conditions. A consultant dermatologist reviewed patients recruited into the study. Laboratory investigations were be done at the microbiology laboratory in KNH and Paediatrics Department laboratory, UON.

DATA ANALYSIS

Data was entered into computer software, SPSS version 12.0.1. Data was cleaned by running frequencies and all errors were corrected using the original data collection tool. Descriptive statistics were carried out for both continuous and categorical variables. Measures of central tendency and dispersion were used to summarise continuous data (CD4 count, CD4%, age). Frequency distribution and proportions were used for categorical variables (sex, skin condition presence). An independent T- test was used to determine differences in the mean CD4% among HIV infected children with a skin condition and those without. Chi-square test was used to determine significant differences between HIV infected and uninfected children in regard to the key variables. Odds ratio was calculated to compare the odds of skin manifestations between HIV infected and uninfected children. Significance levels were set at $\alpha = 0.05$

ETHICAL CONSIDERATIONS

Permission to conduct the study was obtained from the KNH Ethics and Research Committee. Informed written consent was obtained from the parents/ legal guardians of all participants after the scientific value and applications of the study were elucidated. Patient identities were kept confidential and this entailed taking care to ensure that photographs taken did not reveal the identity of the child. Participation was voluntary and no extra cost was incurred by the patient during the course of the study. No patient was denied regular medical attention. Information obtained in the course of the study was availed to primary clinicians for the day to day care of the patients.

RESULTS

Of the 100 HIV infected children, 53 were male and 47 were female, with a median age of 2.8 years (IQR 1.1-7.0). Of the 100 controls, 61 were male and 39 were female, with a median age of 2.9 years (IQR 1.4-7.0). There was no significant difference between the proportion of males to females among cases and controls (P=0.25). There was no significant difference in the ages between the HIV infected and uninfected children (P=0.86). There was a significant difference in the growth parameters of the HIV infected children and HIV uninfected children (Z scores of <0.006). [Table 2]

Table 2: Background characteristics of the study population

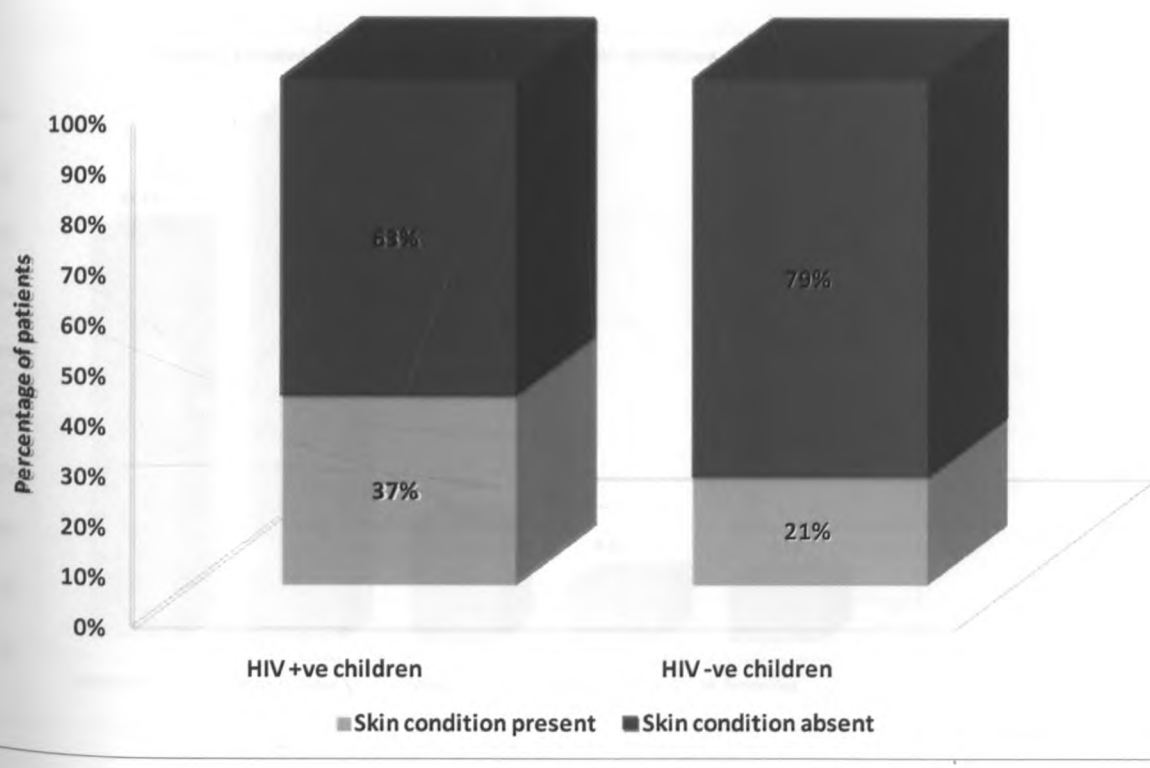
Variable	HIV infected children N=100 [%]	HIV negative children N=100 (%)	P
Male	53 (53)	61 (61)	0.25
Female	47 (47)	39 (39)	
M: F ratio	1.13:1	1.56:1	
Age (yr) median (IQR)	2.8 IQR (1.1-7.0)	2.9 IQR (1.4-7.0)	0.86
Nutrition Status			
Weight for age Z score (WAZ) Mean(SD)	-1.65(0.61)	-1.01(0.53)	<0.001
Weight for height Z score(WHZ) Mean(SD)	-1.24(0.97)	-0.88(0.84)	0.006
Height for age Z score(HAZ) Mean(SD)	-1.05(0.65)	-0.57(0.66)	<0.001

The prevalence of skin conditions in HIV infected children was 37% (95% CI 27.5%-46.5%) and in uninfected children 21% (95%CI 13.0-29.0%). The Odds Ratio was 2.2 (95%CI 1.2-4.1). The prevalence of skin conditions among HIV infected children was significantly higher than in HIV uninfected children (P=0.01) [Table 3, Figure 1].

Table 3: Prevalence of skin disease in the study population

Variable	HIV infected children	HIV negative children	OR (95% CI)	P
Any skin condition	**37% (95%CI 27.5%- 46.5%)**	**21% (95%CI 13.0% - 29.0%)**	2.2(1.2 – 4.1)	0.01

Figure 1: Prevalence of skin conditions among HIV infected and uninfected children



The most common skin conditions among HIV infected children (cases) were infections followed by eczematous dermatitis while in the HIV uninfected children (controls) it was eczematous dermatitis followed by infections. [Figures 2 and 3]

Figure 2: Prevalence of common skin conditions in HIV infected children

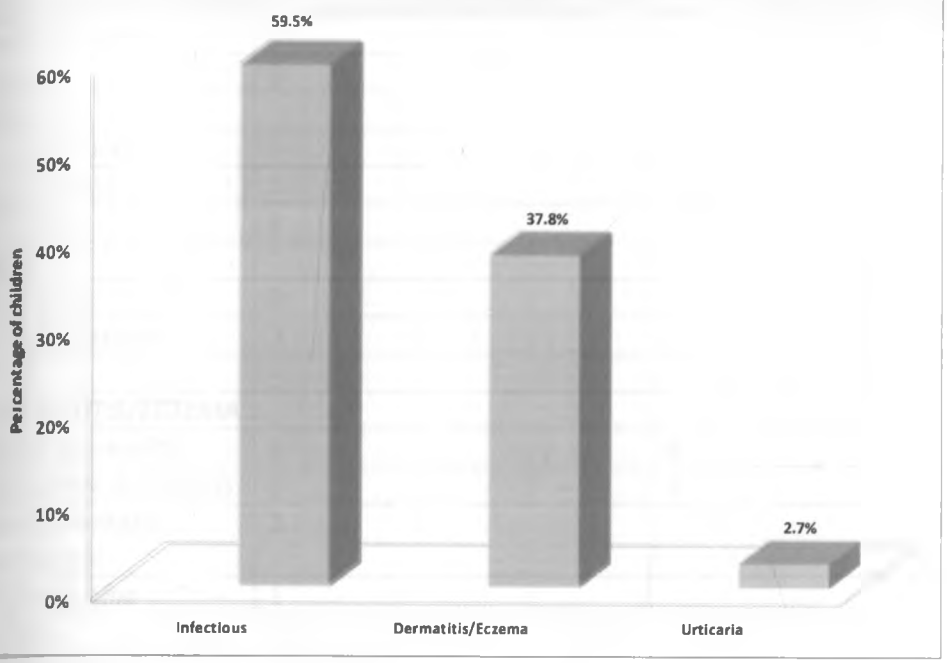


Figure 3: Prevalence of common skin conditions in HIV -ve children

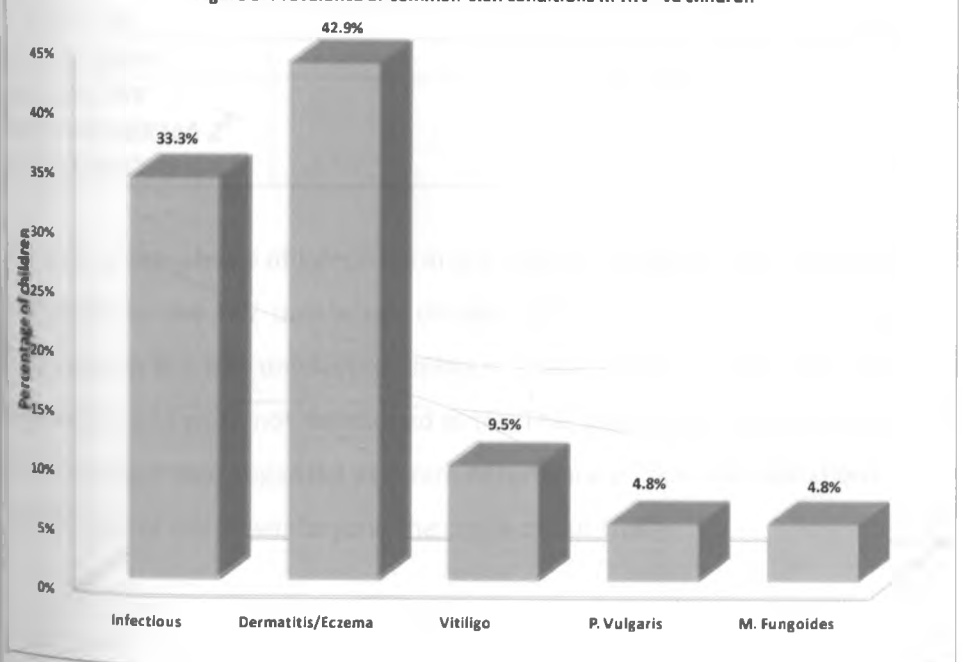


Table 4: Dermatological disease in HIV infected and HIV sero-negative children

Variable	HIV infected children with dermatological disease N=37	HIV negative children with dermatological disease N=21
INFECTIOUS		
Fungal	9	5
Bacterial		
Folliculitis	4	2
Abscess	1	
SSSS	2	
Viral		
Warts	3	
Molluscum	3	
DERMATITIS/ECZEMA		
Atopic dermatitis	6	6
Seborrheic dermatitis	3	2
Contact irritant dermatitis	3	
Pityriasis alba	1	
Xerosis	1	
Keratosis pilaris		1
URTICARIA	1	
VITILIGO		2
P.VULGARIS		1
M.FUNGOIDES		1
EXFOLIATIVE ERYTHRODERMA 2^{0} TO ICHTHYOSIS		1

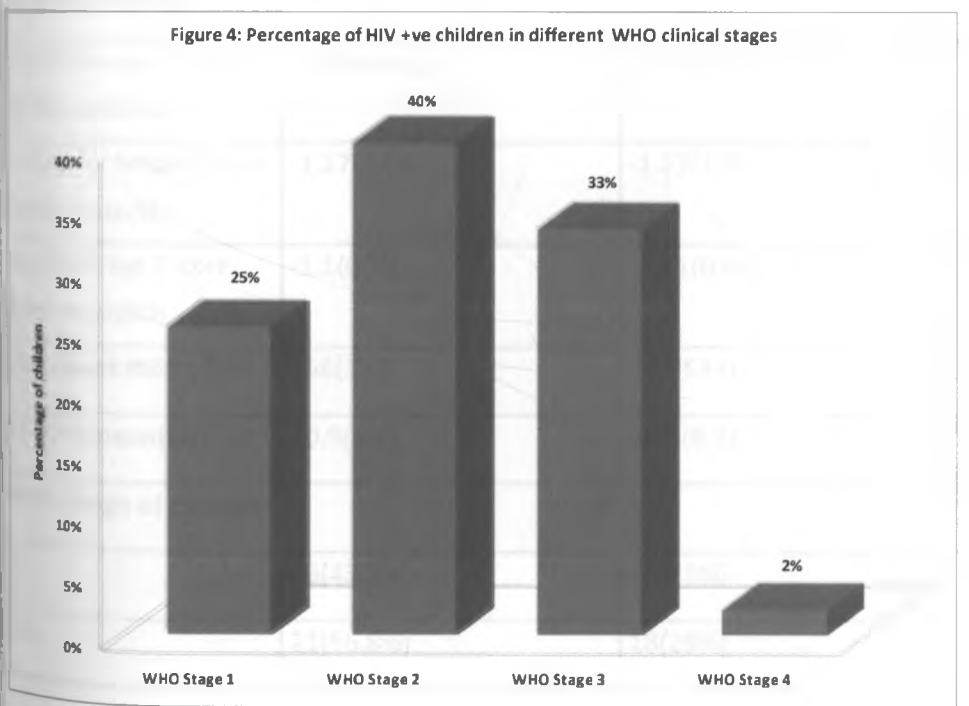
The higher prevalence of infections in HIV infected children could be due to relative immunosuppression as compared to the HIV uninfected children. Of note is the findings of pemphigus vulgaris and mycoses fungoides in the HIV uninfected children. These conditions are extremely rare in the general paediatric population and were not mentioned in the Thai studies that evaluated HIV infected children. Their finding in our study is thus regarded as a rare occurrence of skin manifestations in the paediatric population, the significance of which was beyond the scope of our study.

Among the HIV infected children, the median CD4 count and percent was 523(IQR 305-900) and 14(IQR 8.5-18.8) respectively. Majority of the children (53%) were severely immunosuppressed and the distribution according to WHO clinical stage is also represented. [Table 5 and Figure 4]

Table 5: Clinical characteristics of the HIV infected children

Variable	HIV infected children N=100	%
CD4 count (median)	523 (IQR 305-900)	
CD4 (%) (median)	14 (IQR 8.5-18.8)	
≥25 (no immunosuppression)	10	10
15-24 (moderate immunosuppression)	37	37
1-14 (severe immunosuppression)	53	53
WHO Stage of disease		
1	25	25
2	40	40
3	33	33
4	2	2

Figure 4: Percentage of HIV +ve children in different WHO clinical stages



The majority of the HIV infected children recruited into our study had more advanced disease probably because most of them were recruited from the wards and had been admitted for other reasons and hence had relatively higher levels of immunosuppression.

Among the HIV infected children, there was no significant difference in age or male: female ratio when those with a skin condition were compared to those without. There was also no significant difference in the growth parameters. However, there was a significant difference in the CD4 count (P=0.003) and CD4% (P=0.001) when comparing the two groups. The HIV infected children with skin disease were also significantly more likely to have advanced HIV disease (P=0.005). [Table 6]

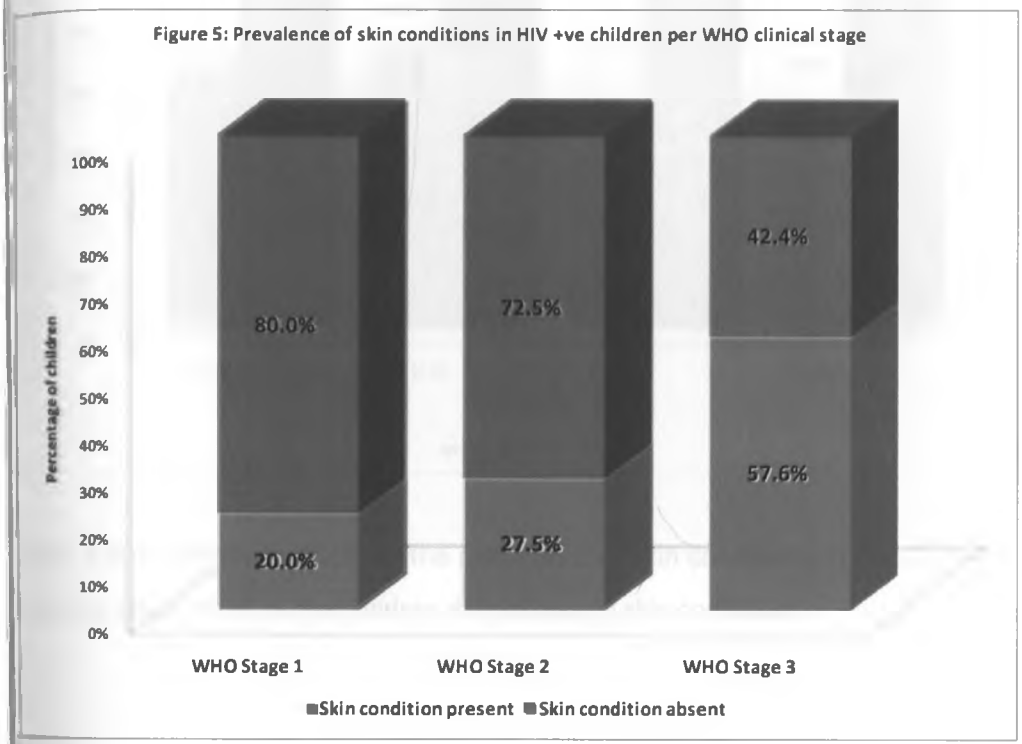
Table 6: Comparison of HIV infected children with skin disease to those without

Variable	HIV infected children with dermatological disease N=37	HIV infected children without dermatological disease N=63	OR (95%CI)	P
Male	19	34	1.11(0.46-2.71)	0.800
Female	18	29		
M:F ratio	1.06:1	1.17:1		
Age(mo) (mean)	3.9(4)	4.3(3.5)		0.650
Nutrition Status				
Weight for age Z score (WAZ) Mean(SD)	-1.66(0.61)	-1.64(0.62)		0.89
Weight for height Z score (WHZ) mean(SD)	-1.27(0.93)	-1.22(1.0)		0.85
Height for age Z score (HAZ) mean(SD)	-1.1(0.59)	-1.01(0.69)		0.85
CD4 count mean (SD)	458(336)	757(533)		0.003
CD4(%) mean(SD)	10.9(5.8)	16.5(8.2)		0.001
WHO Stage of disease				
1-2	16(43.2%)	49(71%)		
3-4	21(56.8%)	18(29%)	1.99(1.23-3.21)	0.005

This was a significant finding as presence of skin manifestations in HIV infected children was associated with more advanced disease. Although the study was not designed to examine causal relationship between presence of skin manifestations and HIV infection, it demonstrated some association between severity of HIV and presence of skin conditions.

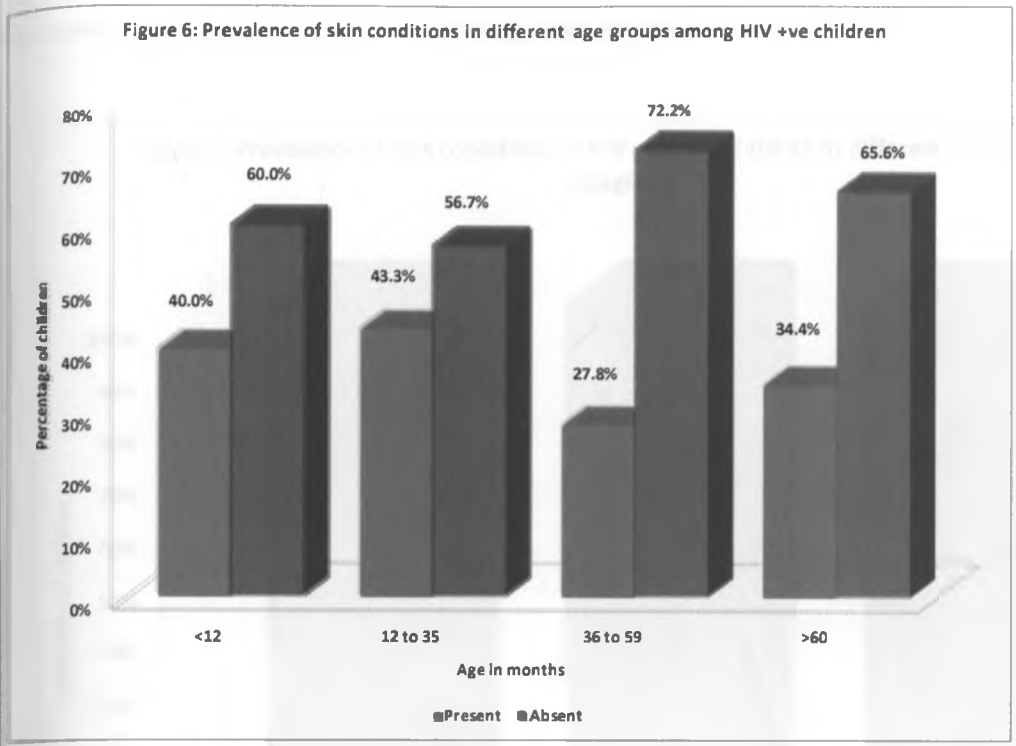
The prevalence of skin conditions increased with advancement of HIV disease as evidenced by Figure 5.

Figure 5: Prevalence of skin conditions in HIV +ve children per WHO clinical stage



This trend is similar to that in the Thai studies where the prevalence of cutaneous manifestations increased with increased levels of immunosuppression.[57]

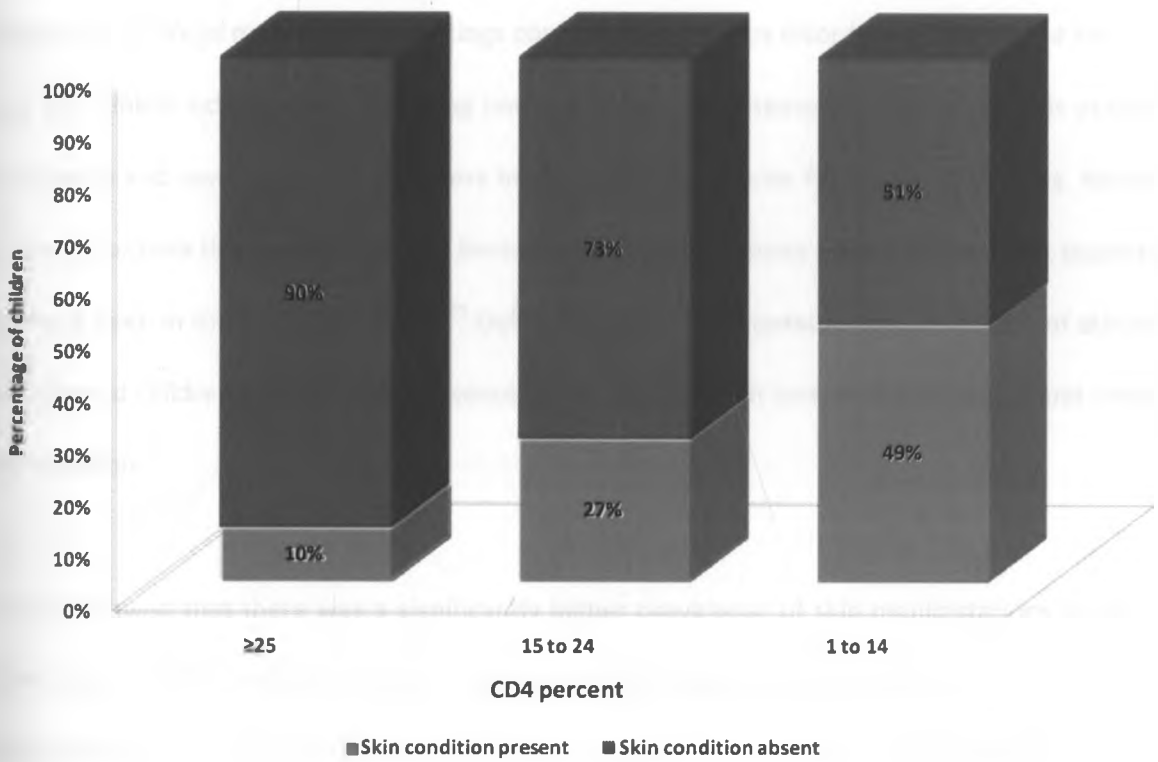
prevalence of skin conditions among the different age groups in the HIV infected children is represented in Figure 6.



There was no obvious pattern in the prevalence of skin conditions in the different age groups although in each age group more of the children did not have a skin condition.

The prevalence of skin conditions increased with decreased immunological status among the HIV infected children. [Figure 7] Again this compares with the findings in the Thai studies.[57] There seems to be a relationship between increased immunosuppression and increased prevalence of skin conditions.

Figure 7: Prevalence of skin conditions in HIV positive children in different immunological categories



DISCUSSION

Skin manifestations are hallmarks of HIV infection and are seen at every stage of HIV/AIDS and are often the initial presentation in most instances. Several studies on dermatological findings and CD4 cell counts in HIV/AIDS patients in the Western world are in existence and have shown the importance of cutaneous disorders as useful markers of disease progression.[50,63] As the search for reliable clinical indicators for management of HIV in resource-poor settings continues, cutaneous disorders of HIV should be considered among key clinical indicators of underlying immune status and disease progression.[9,10] It is observed that the incidence and severity of skin disorders increase as the immune function deteriorates. Nevertheless, data to substantiate this relation remains limited especially in resource poor settings. Most studies done in Africa have been in the adult population.[47] Our study aimed to determine the prevalence of skin disorders in HIV infected children and correlate presence of skin disease with immunological status and clinical stage of HIV infection.

Our study showed that there was a significantly higher prevalence of skin manifestations in HIV infected children than in HIV uninfected children. Skin conditions being approximately twice as common in HIV infected children, has an important impact on health policies, parental and health worker awareness. Our study demonstrated that among the HIV infected children, skin disease was associated with advanced HIV disease. Of important note is that there was no significant difference in the anthropometric parameters of the HIV infected children with skin disease and those without skin disease. Our study also demonstrated that there was a significantly higher prevalence of skin conditions as the level of immunosuppression increased among the HIV infected children. These findings show a similar trend found in studies done in Thailand. [56.57]

Our study was hospital based and this could have had an impact on the skin conditions seen in the HIV uninfected children recruited from the paediatric wards and not an out-patient setting. In our study, among the skin conditions in the HIV infected children, infections were most prevalent (59.5%) followed by eczematous skin lesions (37.8%). Among the infections, fungal infections were found to predominate followed by bacterial infections. In the HIV negative children, the most prevalent skin condition was eczematous dermatitis (42.9%) followed by infections (33.3%). In the Thailand study, infections were also found to the most prevalent skin condition among HIV infected children of which fungal causes predominated.[57]

Fungal infections were found to be more prevalent among the HIV infected children as compared to the uninfected children. The fungal infections were tinea corporis [photo 7] and tinea capitis [photo 8]. Our study found a prevalence of 24% among HIV-infected children and 13% in the HIV-uninfected children. In the Thai study the prevalence of fungal infections was found to be 12%.[57] The difference could be due to environmental, racial and genetic factors. Bacterial skin conditions included staphylococcal scalded skin syndrome (SSSS) [photos 11-12], folliculitis [photo 15] and abscess [photos 14]. SSSS was associated with severe immunosuppression. A study done in Thailand demonstrated a prevalence of 6.7% for bacterial infections while in our study prevalence was 7%.[57] Other studies have also demonstrated that common bacterial infections in HIV infected children include folliculitis, impetigo, abscess, cellulitis and furunculosis and staphylococcus aureus was the most common pathogen in HIV infected patients.[69]

Molluscum contagiosum was found in 8.1% of the cases [photo 6]. Molluscum contagiosum is generally found in patients who have deficient cellular immunity and this was demonstrated in our study in which none of the HIV uninfected children manifested this condition. Verrucae plana were found in 7.7% of the HIV infected children [photo 13]. Predisposing conditions for more extensive involvement include atopic dermatitis and any condition in which there is decreased cell-mediated immunity (eg, AIDS, organ transplantation). Common warts were absent in our controls similar to a study done in Nigeria. This is

difficult to explain, as warts are usually more common in children of school age. It appears however, from data derived by other studies in Africa, that warts are less common in African children as compared to White people.[70]

The prevalence of eczematous dermatitis in HIV infected children was 6% [photos 1-4], that of papular urticaria was 3.8% [photos 9-10] while that of seborrheic dermatitis was 3.8% [photos 1-2]. The prevalence of seborrheic dermatitis in HIV infected children was 4.5% in the Thailand study.[57] Socioeconomic and environmental factors may account for the slight difference in prevalence.

There were a few rare conditions that we encountered in the HIV uninfected children in our study; pemphigus vulgaris [photo 17] and mycoses fungoides [photos 19-20]. Incidence of pemphigus is 0.75 to 5 cases per million per year however, it usually occurs in middle-aged and older persons.[73] Mycoses fungoides represents the most common type of cutaneous T cell lymphoma (CTCL) and accounts for ≈ 50% of all primary cutaneous lymphomas. It derives its name from the mushroom-like appearance of the cutaneous tumor nodules. Incidence is ≈ 6 per million per year. Peak age at presentation is in excess of 55 to 60 years with a 2:1 M: F ratio and is more common in blacks.[74] A study done by Crowley in younger patients found that majority of the patients were in T1 stage (limited plaque/patch stage) although the long term survival is reduced. These conditions are extremely rare in the general paediatric population and were not mentioned in the Thai studies that evaluated HIV infected children. Their finding in our study is thus regarded as a rare occurrence of skin manifestations in the paediatric population, the significance of which was beyond the scope of our study.

CONCLUSIONS

1. Skin conditions were significantly more prevalent in HIV infected children as compared to HIV negative children.
2. Skin conditions were significantly more prevalent in children with increasing WHO clinical stage
3. HIV infected children with a skin condition had significantly lower CD4% than those without a skin condition

REFERENCES

1. Joint United Nations Programme on HIV/AIDS and World Health Organization. Report on the Global HIV/AIDS Epidemic, June 2006. UNAIDS, WHO; 2006.
2. National AIDS and STI control programme, Ministry of Health Kenya. AIDS in Kenya. 7th ed: NASCOP 2005 pg 1-3.
3. Singh A., Georgalas C and Patel N. ENT manifestations in children with HIV infection. *Clin Otolaryngol Allied Sci* 2003; 28: 240 – 243.
4. Aftergut K and Cockerell CJ. Update on the cutaneous manifestations of HIV infection. *Dermatol Clin* 1999; 17: 445–471.
5. Friedman-Kien AE, Laubenstein L and Marmor M. Kaposi's sarcoma and Pneumocystis pneumonia among homosexual men — New York City and California. *MMWR Morb Mortal Wkly Rep* 1981; 30:305-8.
6. Dover JS and Johnson RA. Cutaneous manifestations of human immunodeficiency virus infection. Part II. *Arch Dermatol* 1991; 127:1549–58.
7. Centers for Disease Control Prevention. Revision of the CDC surveillance case definition for acquired immunodeficiency syndrome. MMWR 1987; 36(Suppl. 1):3S–15S.
8. Centers for Disease Control Prevention. Revised classification system for HIV-1 infection in children less than 13 years of age. MMWR 1994; 43:1–13.
9. Njoku MO, Sirisena ND, Idoko JA, Jelpe D. CD4 T-lymphocyte counts in patients with human immunodeficiency virus type 1 (HIV-1) and healthy populations in Jos, Nigeria. *Niger Postgrad Med J* 2003; 10: 135–139.
10. Akinola NO, Olasode O, Adediran IA, *et al* . The search for a predictor of CD4 cell count continues: total lymphocyte count is not a substitute for CD4 cell count in the management of HIV-infected individuals in a resource-limited setting. *Clin Infect Dis* 2004; 39: 579–581.
11. Jura E, Chadwick G, Josephs S, Steinberg S and Yogev R. 1989. Varicella-zoster virus infections in children infected with human immunodeficiency virus. *Pediatr. Infect. Dis. J.* 8:586–590.
12. Patterson L, Butler K and Edwards M. 1989. Clinical herpes zoster shortly following primary varicella in two HIV-infected children. *Clin. Pediatr.* 28:354.
13. Colebunders R, Mann J and Francis H.1988. Herpes zoster in African patients: a clinical predictor of HIV infection. *J. Infect. Dis.* 157: 314–318.
14. Kosuge H. HHV-6, 7 and their related diseases. *J Dermatol Sci* 2000; 22:205-12.

15. Siegfried E. Human papillomavirus screening in pediatric victims of sexual abuse. *Pediatrics* 1998; 101:43-7.

16. Thiboutot DM. Cytomegalovirus diaper dermatitis. *Arch Dermatol* 1991;127:396-98.

17. Berger RS, Stoner MF, Hobbs ER and Hayes TJ. Cutaneous manifestations of human immunodeficiency virus exposure. *J Am Acad Dermatol* 1988; 19:298-303.

18. Marino CT, McDonald E and Romano JF. Seborrheic dermatitis in acquired immunodeficiency syndrome. *Cutis* 1991; 50: 217-8.

19. Barton JC and Buchness MR. Nongenital dermatologic disease in HIV-infected women. *J Am Acad Dermatol* 1999; 40: 938–948.

20. Prose N. HIV infection in children. *J Am Acad Dermatol* 1990; 22: 1223–1231.

21. Mahe A, Boulais C and Blanc L. Seborrheic dermatitis as a revealing feature of HIV infection in Bamako, Mali [letter]. *Int J Dermatol* 1994; 33: 601–602.

22. Mahe A, Simon F and Coulibaly S. Predictive value of seborrheic dermatitis and other common dermatoses for HIV infection in Bamako, Mali. *J Am Acad Dermatol* 1998; 38: 1084–1086.

23. Eisenstat BA and Wormser GP. Seborrheic dematitis and butterfly rash in AIDS [letter]. *N Engl J Med* 1984; 311: 189.

24. Soeprono FF, Schinella RA and Cockerell CJ. Seborrheic-like dermatitis of acquired immunodeficiency syndrome. A clinicopathologic study. *J Am Acad Dermatol* 1986; 14 (2 Part 1): 242–248.

25. Hamann ID. Non-infection mucocutaneous presentations of human immunodeficiency virus infection. *Australas J Dermatol*. 1997; 38: 105-12.

26. Helton JL. Genital dermatology in the HIV-infected patient. *AIDS Patients Care*. STDs. 1997; 11: 237-43.

27. Mallon E. HIV-associated psoriasis. *AIDS Patient Care*. STDs. 2000; 18:509-20.

28. Liautaud B, PapeJW and DeHovitz JA. Pruritic skin lesions: a common initial presentation of acquired immunodeficiency syndrome. *Arch Dermatol*. 1989; 125:629-632. Beral V, Peterman TA, Berkelman RL and Jaffe HW. Kaposi's sarcoma among persons with AIDS: a sexually transmitted infection? *Lancet* 1990; 335: 123-8.

29. Colebunders R, Mann JM and Francis H. Generalized papular pruritic eruption in African patients with HIV infection. *AIDS*. 1987;1: 117-121.

30. Pallangyo KJ. Cutaneous findings associated with HIV disease including AIDS: experience from Sub Saharan Africa. *Trop Doct*. 1992; 22(suppl 1):35-41.

31. Beral V, Peterman TA, Berkelman RL and Jaffe HW. Kaposi's sarcoma among persons with AIDS: a sexually transmitted infection? *Lancet* 1990; 335: 123-8.

32. Smith KJ, Skelton HG and Yaeger J et al. Cutaneous findings in HIV-1 positive patients: a 42-month prospective study. *J Am Acad Dermatol* 1994: 31: 746–754.

33. Greenspan D. Oral manifestations of primary and acquired immunodeficiency diseases in children. *Pediatr Dent* 1987;9: 98-194.

34. Johnson RA. Dermatophyte infections in human immune deficiency virus (HIV) disease. *J Am Acad Dermatol* 2000:43 (5 Suppl.): S135–S142.

35. Dimino-Emme L and Gurevitch AW. Cutaneous manifestations of disseminated cryptococcosis. *J Am Acad Dermatol* 1995:32 (5): 844–850.

36. Garman ME and Tyring SK. The cutaneous manifestations of HIV infection. *Dermato/Clin* 2002: 20: 193–208.

37. Miller HE, Keddie FM and Johnstone HG. Histoplasmosis: cutaneous and mucomembranous lesions, mycologic and pathologic observations. *Arch Dermatol Syphilol* 1947: 56:715.

38. Cohen PR, Bank DE and Silvers DN. Cutaneous lesions of disseminated histoplasmosis in human immunodeficiency virus-infected patients. *J Am Acad Dermatol* 1990: 23: 422.

39. Pappas P. Blastomycosis in the immunocompromised patient. *Semin Respir Infect* 1997: 12: 243–251.

40. Ungpakom R. Cutaneous manifestations of Penicillium marneffei infection. *Curr Opin Infect Dis* 2000: 13: 129–134.

41. Duong TA. Infection due to Penicillium marneffei, an emerging pathogen: review of 155 reported cases. *Clin Infect Dis* 1996: 23: 125–130.

42. Flores G, Stavola JJ, Noel GJ. Bacteremia due to Pseudomonas aeruginosa in children with AIDS. *Clin Infect Dis* 1993; 16:706-8.

43. Krasinski K, Borkowsky W, Bonk S, Lawrence R, Chandwani S. Bacterial infections in human immunodeficiency virus-infected children. *Pediatr Infect Dis J* 1988; 7:323-8.

44. Kumar B, Rai R and Kaur I. Childhood cutaneous tuberculosis: a study over 25 years from northern India. *Int J Dermatol* 2001; 40: 26–32.

45. Yinnon, A. M. and Coury-Doniger P. 1996. Serologic response to treatment of syphilis in patients with HIV. *Arch. Intern. Med.* 156:321–325.

46. Whitworth JM, Janniger CK, Oleske JM and Schwartz RA. Cutaneous manifestations of childhood acquired immunodeficiency syndrome and human immunodeficiency virus infection. *Cutis* 1995; 55: 62–6, 70–2.

47. Edith N and Anisuiba B. Correlation of mucocutaneous manifestations of HIV/AIDS infection with CD4 counts and disease progression. *Int J Dermatol* 2007; 46: 14–18.

48. Boon-Kee G, Chan K, Sen P and Patton N. Spectrum of skin disorders in human immunodeficiency virus-infected patients in Singapore and the relationship to CD4 lymphocyte counts. *Int J Dermatol* 2007; 46: 695–699.

49. Viroj W. Prevalence of dermatological disorders in Thai HIV-infected patients correlated with different CD4 lymphocyte count statuses. *Int J Dermatol* 2007; 43: 265–268.

50. Jing W, Ismail R. Mucocutaneous manifestations of HIV infection: a retrospective analysis of 145 cases in a Chinese population in Malaysia. *Int J Dermatol* 1999; 38 : 457–463.

51. Krishnam R, Ramani T and Vandana S. Skin disease: clinical indicator of immune status in human immunodeficiency virus infection. *Int J Dermatol* 2005; 44: 646–649.

52. Shearer WT, Quinn TC and LaRussa P. Viral load and disease progression in infants infected with human immunodeficiency virus type 1. Women and Infants Transmission Study Group. *N Engl J Med* 1997; 33:1337–42.

53. Tovo PA, de Martino M and Gabiano C. Prognostic factors and survival in children with perinatal HIV-1 infection. The Italian Register for HIV Infections in Children. *Lancet* 1992; 339:1249–53.

54. Bakari M, Lyamuya E and Mugusi F. The prevalence and patterns of skin diseases in relation to CD4 counts among HIV-infected police officers in Dar es Salaam. *Trop Doct* 2003; 33: 44–48.

55. Nance KV, Smith ML and Joshi VV. Cutaneous manifestations of acquired immunodeficiency syndrome in children. *Int J Dermatol* 1991; 30:531–9.

56. Siriwan Wananukul. MD. Mucocutaneous findings in pediatric AIDS. *Pediatric dermatology* 1999; 16: 359-363.

57. Siriwan Wananukul. MD. Mucocutaneous findings in pediatric AIDS. *Pediatric dermatology* 2003; 20: 289-294.

58. Ogunbiyi A, Owoaje E and Ndahi A. Prevalence of skin disorders in school children in Ibadan, Nigeria. *Pediatr Dermatol* 2005; 22:6-10.

59. Daguatchew Shibeshi. Pattern of skin disease at the Ethio-Swedish Pediatric Hospital, Addis Ababa, Ethiopia. *Pediatr Dermatol* 2000; 17:357-359.

60. Popescu R, Popescu C M, Williams H C and Forsea D). The prevalence of skin conditions in Romanian school children. *Br J Dermatol* 1999; 140:891–896.

61. Inanir I and Sahin M. Prevalence of skin conditions in primary school children in Turkey. *Pediatr Dermatol* 2002; 19:307-311.

62. Fung W and Lo K. Prevalence of skin disorders among school children in a student health service centre in Hong Kong. *Pediatr Dermatol* 2000; 17:440-446.

63. Kumarasamy N, Solomon S and Madhivanan P. Dermatologic manifestations among human immunodeficiency virus patients in south India. *Int J Dermatol* 2000; 39: 192–195.

64. Schmeller W. Community health workers reduce skin diseases in East African children. *Int J Dermatol* 1998;37: 370-7.

65. Schmeller W, Dzikus A. Skin diseases in children in rural Kenya: long-term results of a dermatology project within the primary health care system. *Br J Dermatol* 2001; 144:118-24.

66. Tunnessen WW Jr. A survey of skin disorders in pediatric, general and dermatology clinics. *Pediatric Dermatol* 1984; 1(3):219–222.

67. Bechelli LM, Haddad N, Pimenta WP, et al. Epidemiological survey of skin diseases in school children living in Porus Valley (Acre State, Amazonia, Brazil). *Dermatologica* 1981; 163: 78-93.

68. Lange M, Nowicki R, Baran W and Bykowska B. Dermatophytosis in children and adolescents in Gdansk, Poland. *Blackwell Publishing* Ltd 2004. Mycoses, 47, 326–329.

69. Geusau A, Tschachler E. HIV-related skin diseases. *J R Coll Physicians Lond* 1997; 31:374-9.

70. Dagnew MB, Erwin G. Epidemiology of common transmissible skin disease among primary school children in Northwest Ethiopia. *Trop Geogr Med* 1991; 43:152–155.

71. Sunil Dogra and Bhushan Kumar. Epidemiology of Skin Diseases in School Children:A Study from Northern India. *Pediatr Dermatol* 2003; 20:470-473.

72. Williams HC. Epidemiology of skin diseases. Champion RH, Burton JL, Burns DA, Breathnach SM,eds. *Textbook of dermatology*,6th ed.Oxford:Blackwell Science,1998:139 –158.

73. Bystryn J and Rudolph J. Pemphigus. *Lancet* 2005; 366:61-73.

74. Criscione V and Weinstock M. Incidence of cutaneous T-cell lymphoma in the United States, 1973-2002. *Arch Dermatol.* 2007; 143:854-9.

APPENDIX I:

CONSENT FORM

Researchers

NAME	POSITION	DEPARTMENT
Polly Okello	Principal Investigator	Pediatrics
Ruth Nduati	Supervisor	Pediatrics
Timothy Munyao	Supervisor	Medicine
Dalton Wamalwa	Supervisor	Pediatrics

Emergency telephone number: Dr. Polly Okello, Department of Paediatrics, University of Nairobi: 0727-014174

Researchers' statement:

We are asking you to volunteer for a research study. Before you decide whether to take part in the study, we would like to explain the purpose of the study. We also want to explain the risks and benefits, and what would be expected of you if you agree to be in the study. It is important that you understand that your participation in this study is voluntary. This form will help you decide if you want to take part in the study. Once you understand the study, you can choose to be a part of the study or not. If you choose to be a part of this study, we will ask you to sign your name or make your mark on this form. We will give you a copy to keep. This process is called informed consent.

It is important that you know the following:

- You do not have to be in this study if you do not want to join.
- You may decide not to take part in the study or to withdraw from the study at any time.
- If you decide not to take part in the study, you can still join another research study later.

PURPOSE OF THE STUDY

HIV stands for human immunodeficiency virus. Having the virus in the body does not necessarily mean that the child is sick. However, over a period of indeterminate duration, the virus causes a weakening of the

body's immune system. This means that the child is more vulnerable to the common diseases of childhood and other diseases that may not be very common. Presence of these diseases and other symptoms attributable to the virus is what we call acquired immunodeficiency syndrome or AIDS.

Skin changes, which may be the initial signs of virus-related immunosuppression, frequently occur in HIV infected children. Recognising HIV-related skin changes may lead to the diagnosis of HIV infection in the early stages which provides early entry into comprehensive care including nutritional support, prophylaxis against common pathogens and subsequently antiretroviral therapy. Skin conditions related to HIV infection may present differently due to differences in race, age, sex and environment. These are well described in Western literature but there is no such description in Kenya. Few studies have been carried out in Africa on skin manifestations of HIV infection in children.

STUDY PROCEDURES

If you decide to participate in the study, you will be asked several questions about the child's health. A doctor will then examine the child. Photographs of the skin condition will be taken. They will not reveal the identity of the child. The photographs will be archived as part of the child's examination findings. Further tests may be necessary to determine the cause of the skin condition including a skin biopsy and scrapings. Blood will also be drawn to evaluate the stage of the child's infection. This will be taken to the laboratory and will help us make a clear diagnosis so that we treat the child appropriately.

RISKS AND/OR DISCOMFORTS

In case a skin biopsy will be required, the procedure may cause slight discomfort to the child and afterward there may be a minimal risk of bleeding or infection. However, we will take the necessary precautions to minimise any risk or discomfort to the child. Pain relief, antibiotic cover and pressure dressing will be available to the child. The child may feel pain when we draw blood for testing and the skin in the area pricked by the needle may be a little sore. There is a rare risk of infection at the place of the needle stick. The amount of blood drawn will depend on the test; CD4 count and percentage - 3mL and HIV-DNA PCR - 1mL.

BENEFITS

If the child is found to have any illness that was not previously diagnosed, we will liase with the doctor who normally sees him to ensure that appropriate and prompt advise and treatment are given. You or others may benefit in the future from information learned in this study. The child will get the benefit of being reviewed by a consultant dermatologist and this will further help in the management of your child's skin condition. While taking part in the study, the child will continue receiving appropriate treatment including care and support related to HIV infection. This care will be paid for by the study and provided by the study staff.

OTHER INFORMATION

COSTS TO YOU

There is no cost to you for being in this study. Treatments available to you from the study will be given free of charge.

CONFIDENTIALITY

Efforts will be made to keep all personal information related to you and the child confidential. Photographs taken will not reveal the identity of the child. Any publication of this study will not use your name or the child's name or identify you or the child personally.

RESEARCH-RELATED INJURY

If you think your child has an injury or illness related to this study, contact the study staff right away. The study staff will treat your child or refer your child for treatment. If your child is injured as a result of being in the study, the study staff will give you immediate necessary treatment for the injuries, free of charge. The study staff also will tell you where you can get additional treatment for the injuries, if needed.

WITHDRAWAL

At any time you are free to withdraw or refuse to participate in the research study.

PROBLEMS OR QUESTIONS

If you ever have any questions about the study you should contact Dr. Polly Okello at KNH on 0727014174. If you have questions about your rights as a research participant, you should contact the Chair of the Kenyatta National Hospital Ethics and Research Committee, at 2726300.

Study participant's statement:

This study has been explained to me. I volunteer to have my child take part in this research. I have had a chance to ask questions. If I have questions later about the research, I can ask one of the researchers listed above. If I have questions about my child's rights as a research subject, I can call the KNH Ethics and Research Committee at 2726300. I give permission to the researchers to use my medical records as described in this consent form. I will receive a copy of this consent form if I would like to.

_____	_____
Participant Name (print)	Date

_____	_____	_____
Parent/Guardian Name (print)	Parent Guardian Signature	Date

_____	_____	_____
Researcher's Name (print)	Researcher's Signature	Date

_____	_____	_____
Study Staff Conducting Consent Discussion (print)	Study Staff Signature	Date

Copies to: 1. Investigators 2. Study participant

APPENDIX II:

QUESTIONNAIRRE/ RECORD SHEET:

Date [ ] [ ] [ ]

Source [ ] out-patient (CCC) = 1 in-patient (ward) = 2

Clinic/Ward number [ ] [ ] [ ] [ ] [ ] [ ]

Study number [ ] [ ] [ ]

Sex [ ] Male = 1 Female = 2

Age Years [ ] Months [ ]

MEDICAL HISTORY

1. Any history of skin lesion(s) prior to diagnosis of HIV? [ ] Yes=1 No=2
2. If yes, what was the age of onset of the skin lesion(s)?
3. Age of onset Years [ ] Months [ ]
4. Was the child on any medication prior to appearance of the skin lesion(s)? [ ] Yes=1 No=2
5. If yes, which medication? _____
6. What body part(s) was involved? Code: involved = 1 uninvolved = 2
    a. Face [ ]
    b. Extremities [ ]
    c. Scalp [ ]
    d. Trunk [ ]
    e. Neck [ ]
7. What was the course of the disease? [ ] Intermittent=1 Continuous=2
8. Was the lesion pruritic (itchy)? [ ] Yes=1 No=2
9. What treatment was given? [ ] Yes=1 No=2
    a. Emollient [ ]
    b. Topical corticosteroid [ ]
    c. Topical immunomodulators
        i. Tacrolimus [ ]
        ii. Pimecrolimus [ ]

d. Phototherapy [ ]

e. Systemic corticosteroids [ ]

f. Topical antifungal [ ]

g. Topical antibiotic [ ]

h. Antihistamine [ ] oral = 1 topical = 2

i. Other (specify) .....

10. What was the response to treatment? [ ]

a. Code: quick improvement =1

b. Code: slow improvement =2

c. Code: worsened =3

d. Code: no change =4

11. When was HIV diagnosed in the child? [ ]

a. Code: 0 to 7 days ago =1

b. Code: 8 to 14 days ago =2

c. Code: 15 to 30 days ago =3

d. Code: more than 30 days ago =4

12. Any medical records documenting presence of skin lesions at diagnosis of HIV? [ ]

a. Yes=1 No=2

13. If yes, what body part(s) was involved? Code: involved=1 uninvolved=2

a. Face [ ]

b. Extremities [ ]

c. Neck [ ]

d. Scalp [ ]

e. Trunk [ ]

14. Was the lesion pruritic? [ ] Yes=1 No=2

15. What treatment was given? Yes=1 No=2

a. Emollient [ ]

b. Topical corticosteroid [ ]

c. Topical immunomodulators

i. Tacrolimus [ ]

ii. Pimecrolimus [ ]

d. Phototherapy [ ]

e. Systemic corticosteroids [ ]

f. Other: (specify) .....

16. What was the response to treatment? [ ]

a. Code: quick improvement (less than 2 weeks) =1

b. Code: slow improvement (more than a month) =2

c. Code: worsened =3

d. Code: no change =4

17. Have CD4 counts been done? [ ] Yes=1 No=2

18. If yes, what were the initial CD4 counts? [ ]

a. Code: < 200 =1

b. Code: 200-349 =2

c. Code: 350-499 =3

d. Code: > 500 =4

19. What other medications is the child on? [ ][ ][ ][ ]

a. Code: Cotrimoxazole =1

b. Code: Dapsone prophylaxis =2

c. Code: Fluconazle prophylaxis =3

d. Code: Supportive treatment(multivitamins, analgesics, hematinics) =4

e. Other (specify) _____

20. When did the skin condition appear in relation to start of any of the above medications? [ ] Before = 1 After = 2

SYSTEMIC ENQUIRY

Central nervous system:

.....

.....

Respiratory system:

.....

.....

Cardiovascular system .....

.....

Gastrointestinal system .....

.....

Genito-urinary system .....

.....

Haematological diseases

.....

.....

Endocrine system

.....

.....

EXAMINATION FINDINGS:

Height (cm) _____

Weight (kg) _____

Head circumference (cm) _____

Left upper mid arm circumference (cm) _____

Z score (SD) _____

Oedema

Present [ ] Yes=1 No=2

Lymphadenopathy

Present [ ] Yes=1 No=2

Generalised ☐

Localised ☐

Specify .....

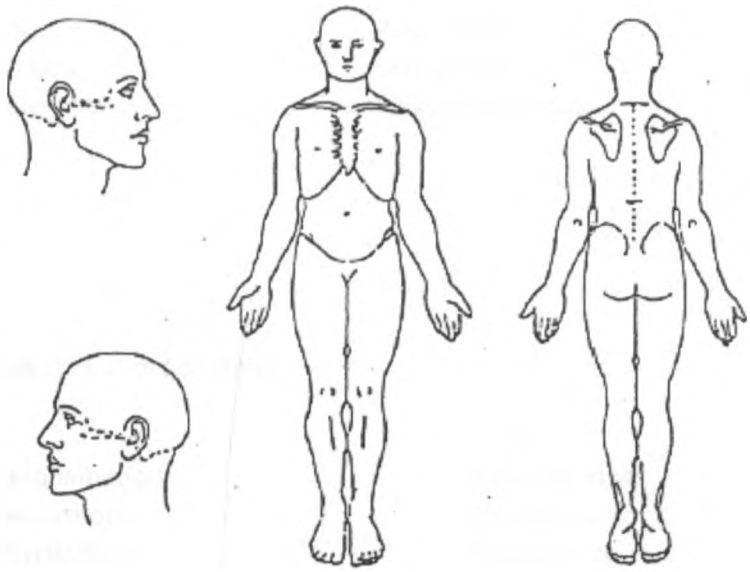
Oral candidiasis

Present [ ] Yes=1 No=2

CUTANEOUS EXAMINATION: (appendix VII)

Distribution of the lesion(s) (tick appropriately):

Acral	☐	Koebnerised	☐
Blaschko's lines	☐	Photosensitive	☐
Dermatomal	☐	Pressure areas	☐
Extensor	☐	Seborrheic	☐
Flexural	☐	Symmetrical	☐
Follicular	☐	Truncal	☐
Generalised	☐	Unilateral	☐
Herpetiform	☐		



Configuration of the lesion(s) (tick appropriately):

Nummular	☐
Linear	☐
Target	☐
Gyrate	☐
Annular	☐

Colour of the lesion(s) (tick appropriately):

Carotenaemia	☐	Jaundice	☐
Hyperpigmentation	☐	Erythema	☐
Hypopigmentation	☐	Erythroderma	☐
Leukoderma	☐	Telangiectasia	☐
Infarcts	☐	Purpura	☐

Morphology of the lesion(s) (tick appropriately):

Macule	☐		
Patch	☐		
Papule			
Acuminate	☐	Pedunculated	☐
Dome-shaped	☐	Sessile	☐
Filiform	☐	Umbilicated	☐
Flat-topped	☐	Verrucous	☐
Oval or round	☐		
Nodule	☐		
Cyst	☐		
Plaque			

Annular	☐	Polymorphic	☐
Arcuate	☐	Serpiginous	☐
Polygonal	☐	Poikilodermatous	☐

Vesicle ☐
Pustule ☐
Bulla ☐
Abscess ☐
Weal ☐

Skin surface (tick appropriately):

Scaling

Desquamation	☐	Hyperkeratotic	☐
Psoriasiform	☐	Exfoliation	☐
Pityriasiform	☐	Maceration	☐
Lichenoid	☐	Verrucous	☐

Secondary changes (tick appropriately):

Lichenification	☐	Fungating	☐
Crusting	☐	Granulation tissue	☐
Dystrophy	☐	Ulcer	☐
Excoriation	☐	Granuloma	☐
Erosion	☐	Hypertrophy	☐
Fissure	☐		

SYTEMIC EXAMINATION:

Central nervous system:

Neck stiffness [ ] Yes=1 No=2
Kernigs sign [ ] positive=1 negative=2
Lateralising signs [ ] Yes=1 No=2
Change in gait [ ] Yes=1 No=2
Other (specify)
.....
.....

ENT

Ear discharge [ ] Yes=1 No=2
Pharyngitis [ ] Yes=1 No=2

Other (specify)
.....
.....

Respiratory system

Respiratory rate (breaths/min): _____

Chest expansion

Symmetrical	☐
Asymmetrical	☐

Rhonchi

Inspiratory	[ ] Yes=1 No=2
Expiratory	[ ] Yes=1 No=2

Crepitations

Left	Anterior	[ ] Yes=1 No=2
	Posterior	[ ] Yes=1 No=2
Right	Anterior	[ ] Yes=1 No=2
	Posterior	[ ] Yes=1 No=2

Other (specify)

.....

Cardiovascular system:

Pulse rate (beats/min): _____

Heart sounds	Normal	[ ] Yes=1 No=2
	Any added sounds	[ ] Yes=1 No=2

Other (specify)

.....

Gastrointestinal system:

Liver palpable [ ] Yes=1 No=2
Spleen palpable [ ] Yes=1 No=2

Other (specify)

.....

Genito-urinary system:

Urethral discharge	[ ] Yes=1 No=2
Genital warts	[ ] Yes=1 No=2

Other (specify)

.....

Musculoskeletal system:

Cellulitis [ ] Yes=1 No=2
Other (specify)
.....

WHO clinical Stage: (appendix III) .....

INVESTIGATIONS:

1. CD4 $^{+}$ T – Cell count Date of result [ ] [ ] [ ]
   Absolute: _____ /mm^3
   Percentage: _____
2. Skin biopsy .....(appendix V) Date of result [ ] [ ] [ ]
3. Skin scraping .....(appendix VI) Date of result [ ] [ ] [ ]

Others (specify) .....

CLINICAL DIAGNOSIS OF SKIN LESION: tick appropriately (appendix IV)

Oral candidiasis [ ]
Seborrheic dermatitis [ ]
Atopic dermatitis [ ]
Dermatophyte infection
- Tinea corporis [ ]
- Tinea capitis [ ]
- Tinea cruris [ ]
- Tinea pedis [ ]
- Onychomycosis [ ]

Varicella zoster [ ]
Pruritic Papular Dermatitis [ ]
Molluscum contagiosum [ ]
Herpes simplex [ ]
Kaposi's sarcoma [ ]
Drug eruption [ ]
Furunculosis [ ]
Scabies [ ]
Other: (specify) .....

APPENDIX III:

REVISED WHO CLINICAL STAGING OF PAEDIATRIC HIV/AIDS DISEASE:

WHO Stage I	• Asymptomatic • Persistent generalized lymphadenopathy (PGL) • Hepatosplenomegaly
WHO Stage II	• Papular pruritic eruptions (PPE) • Seborrhoeic dermatitis • Fungal nail infections • Angular cheilitis • Linear gingival erythema • Extensive human papilloma virus (HPV) or molluscum infection (> 5% body area/face) • Recurrent oral ulcerations (> 2 episodes/ 6 months) • Parotid enlargement • Herpes zoster (> 1 episode/12months) • Recurrent or chronic upper respiratory infection (URTI): Otitis media, otorrhoea, sinusitis (> 2 episodes / 6 months).
WHO Stage III	• Unexplained moderate malnutrition (- 2 SD or Z score) not responding to standard therapy. • Unexplained persistent fever (intermittent or constant, > 1 month). • Oral candidiasis (outside the neonatal period). • Oral hairy leucoplakia • Pulmonary tuberculosis • Severe recurrent presumed bacterial pneumonia (> 2 epidodes/12 months) • Acute necrotizing ulcerative gingivitis/periodontitis • Lymphoid interstitial pneumonia • Unexplained anaemia (<8g/dl), netropenia (<1000/MM3) or thrombocytopenia (< 30,000/MM3) for > 1 month. • HIV related cardiomyopathy • HIV related nephropathy
WHO Stage IV	• Unexplained severe wasting as severe malnutrition (- 3 SD or Z score) not responding to standard therapy. • Pneumocystis pneumonia. • Recurrent severe bacterial infections (> 2 episodes/12 months excluding pneumonia). • Chronic orolabial or cutaneous HSV (lasting > 1 month). • Extrapulmonary tuberculosis • Oesophageal candidiasis • Central nervous system toxoplasmosis • Cryptococcal meningitis • Any disseminated endemic mycosis

	• Cryptosporidiosis or isosporiasis (with diarrhea > 1 month) • CMV infection of organ other than liver, spleen, lymph nodes (and onset age > 1 month) • Disseminated mycobacterium disease other than tuberculosis • Candida of trachea, bronchi or lungs • Acquired recto-vesicular fistula • Cerebral or b-cell non Hodgkin lymphoma • Progressive multifocal leucoencephalopathy (PML) • HIV encephalopathy **Presumptive stage 4 diagnosis in HIV-antibody positive children less than 18 months old where virological confirmation of infection is not available.** Two or more of the following; • Oral candidiasis/thrush • Severe pneumonia requiring oxygen • Severe wasting/failure to thrive • Severe sepsis requiring injectable antibiotics

WHO IMMUNOLOGICAL STAGING OF PAEDIATRIC HIV/AIDS DISEASE:

HIV Associated Immunodeficiency	CD4+Count (% CD4+ or absolute count)			
	<12 months	12-35 months (%)	36-59 months (%)	>5 years (Count)
Not significant	>35	>30	>25	>500
Mild	30-35	25-30	20-25	350-499
Advanced	25-29	20-24	15-19	210-349
Severe	<25	<20	<15	<200

APPENDIX IV: DIAGNOSTIC CRITERIA / CASE DEFINITION

ATOPIC DERMATITIS

Hanifin and Rajka Diagnostic Criteria for Atopic Dermatitis (AD)

Major criteria: Must have three or more of:

1. Pruritus
2. Typical morphology and distribution
   - Flexural lichenification or linearity in adults
   - Facial and extensor involvement in infants and children
3. Chronic or chronically-relapsing dermatitis
4. Personal or family history of atopy (asthma, allergic rhinitis, atopic dermatitis)

Minor criteria: Should have three or more of:

1. Xerosis
2. Ichthyosis, palmar hyperlinearity, or keratosis pilaris
3. Immediate (type 1) skin-test reactivity
4. Raised serum IgE
5. Early age of onset
6. Tendency toward cutaneous infections (especially *S aureus* and herpes simplex) or impaired cell-mediated immunity
7. Tendency toward non-specific hand or foot dermatitis
8. Nipple eczema
9. Cheilitis
10. Recurrent conjunctivitis
11. Dennie-Morgan infraorbital fold
12. Keratoconus
13. Anterior subcapsular cataracts
14. Orbital darkening
15. Facial pallor or facial erythema
16. Pityriasis alba
17. Anterior neck folds
18. Itch when sweating
19. Intolerance to wool and lipid solvents
20. Perifollicular accentuation
21. Food intolerance
22. Course influenced by environmental or emotional factors
23. White dermographism or delayed blanch

SEBORRHEIC DERMATITIS

- Chronic skin inflammation.
- History of itching, redness, flaking, skin irritation.
- Physical examination:
  - erythematous patches or plaques with overlying yellow, greasy scales and crusts.
  - Typically symmetrical affecting areas of higher sebaceous gland concentration.
  - Commonly see on: hairy areas of head, forehead, malar area, nasolabial folds, external ear canals, retroauricular creases.
  - May also affect the chest (presternal area), back and intertriginous areas (axillae, navel, groin, inframammary, anogenital).
  - In mild cases, flaking dandruff may be only manifestation.

- More severe cases present with erythematous plaques associated with thicker yellowish powdery or oily scale eventually progressing to erythroderma.

Skin biopsy will only be done if the diagnosis cannot be made clinically.

Scheinfeld NS. Seborrheic dermatitis. *Skinmed* 4(1):49-50 (2005 Jan-Feb).

MOLLUSCUM CONTAGIOSUM:

Primary lesion

- Firm, smooth, umbilicated papules, usually 2-6 mm in diameter (range 1-15 mm) may be present in groups or widely disseminated on the skin and mucosal surfaces. Lesions greater than 15 mm have been described, particularly in patients with AIDS.
- The lesions can be flesh-colored, white, translucent, or even yellow in color.
- The number of lesions varies from 1-20 up to hundreds in some reports.
- Some lesions become confluent to form a plaque.
- Lesions generally are self-limited but can persist for several years.

Diagnosis is will be made on clinical grounds based on appearance of the lesions. Biopsy will only done if diagnosis is uncertain and there is no contraindication to skin biopsy (appendix V). Identification of characteristic intracytoplasmic inclusion bodies in histologic or cytologic preparations is made by hematoxylin and eosin (H&E) staining of biopsy sections.

Gottlieb SL, Myskowski PL: Molluscum contagiosum. *Int J Dermatol* 1994 Jul; 33(7): 453-61

DERMATOPHYTE INFECTION:

- One or multiple patches of alopecia
- Fine scaling with minimal alopecia and associated inflammation
- May be pruritic

Definitive diagnosis involves direct microscopic examination of specimens after potassium hydroxide (KOH) preparation.

Hurwitz S. *Clinical Paediatric Dermatology* 2nd ed. Philadelphia: W.B. Saunders; 1993: 372-86.

VERRUCA PLANA

HPV cannot be cultured.

Definitive diagnosis can be achieved by:

Electron microscopy

Viral DNA identification using Southern blot hybridization used to identify the specific HPV type present in tissue

Polymerase chain reaction may be used to amplify viral DNA for testing.

The above tests are beyond the capacity of this study hence the diagnosis will be made clinically by a dermatologist.

PAPULAR URTICARIA

History: Patients complain of usually chronic or recurrent episodes of a papular eruption that tends to occur in groups or clusters associated with intense pruritus.

Physical:

- Characterized by crops of symmetrically distributed pruritic papules and papulovesicles. The lesions can also appear in an area localized to the site of insect bites.
- Papules may occur on any body part, but they tend to be grouped on exposed areas, particularly the extensor surfaces of the extremities.
- Scratching may produce erosions and ulcerations.
- Secondary impetigo or pyoderma is common.

The search for the cause of urticaria is beyond the scope of this study. Hence additional tests will not be done. Hence diagnosis will be made clinically by a dermatologist.

FOLLICULITIS

Perifollicular pustules

Favour areas with terminal hairs like scalp, beard, axillae, groin, upper trunk, buttocks, thighs

Diagnosis: Culture of pustular contents
Gram stain of pustular contents
KOH
Tzanck smear (if necessary) to rule out herpes simplex folliculitis
Skin scrapings (if necessary) to rule out demodex mites

STAPHYLOCOCCAL SCALDED SKIN SYNDROME:

Prodrome: malaise, fever, irritability, severe tenderness of skin +/- rhinorrhea, conjunctivitis

Starts as erythema (often at the head) spreading within hours to the remainder of the body. Flaccid bullae form and within 1-2 days after which they slough leaving behind moist skin and areas of crust. Perioral crusting and fissuring is frequent. Scaling and desquamation occurs in the next 3-5 days. The diagnosis of SSSS is verified by isolation of staphylococci from a site other than the blisters. Common sites of isolation include the conjunctivae, nasopharynx, or blood. The location of the cleavage plane on Tzank preparation of a skin biopsy specimen differentiates SSSS and TEN. In SSSS, the cleavage is in the granular layer of the dermis, whereas in TEN, the cleavage is at the dermal-epidermal junction. Definitive diagnosis is double immunofluorescence or enzyme-linked immunosorbent assay tests to identify staphylococcal toxins; these tests are beyond the capacity of this study.

KERATOSIS PILARIS:

Lichenified, hyperkeratotic fissured lesions with scaling.

Diagnosis will be made clinically and biopsy will only be done on recommendation of a dermatologist.

PAPULAR PRURITIC ERUPTION OF AIDS:

Nondescript, erythematous eruption on the trunk and extremities.

Lesions : symmetrical in distribution, non follicular, pruritic, sterile papules and pustules

Definitive diagnosis involves histopathologic examination of skin biopsy sections.

Hamann ID. Non infectious mucocutaneous presentations of human immunodeficiency virus infection. *Australas J Dermatol.* 1997;38:105-12.

HERPES SIMPLEX:

Most cases of herpes simplex infection are recognized by the morphologic characteristics of the disease (small, grouped vesicles on erythematous bases, which then become pustules, umbilicate, and later crust). Diagnostic tests are used when vesicles appear in unusual sites and configurations. The Tzanck test is the most commonly used diagnostic tool for detecting a herpes infection. When viewed under the microscope, infected epithelial cells collected

from herpetic vesicles demonstrate typical characteristics. Nuclear changes include centrally located eosinophilic masses surrounded by a clear halo (Cowdry type A bodies), and the cells have a perinuclear ground-glass appearance. Infected cells also fuse to become multinucleated giant cells, which are characteristic of herpes infection. These changes, however, are not unique to herpes simplex. Therefore, the Tzanck test cannot be used to differentiate HSV from varicella-zoster virus. Direct immunofluorescence studies of biopsy specimens from skin, liver, or brain allow more specific detection of the virus. With indirect immunofluorescence, a fourfold rise in IgG titer in paired serum samples is needed to establish a diagnosis of primary herpes. Culture is the most definitive method for detecting herpes infection. For the purposes of this study, due to financial and time constraints and unavailablility of some of the diagnostic techniques, diagnosis will be determined clinically by an experienced dermatologist.

Habif T. The diagnostic manual of herpesvirus infections. Research Triangle Park, NC: Burroughs Wellcome Co, 1995

VARICELLA ZOSTER:

The appearance of herpes zoster is sufficiently distinctive that a clinical diagnosis is usually accurate. However, the location or appearance of the cutaneous lesions may be atypical in immunocompromised patients and thus require laboratory confirmation. Viral culture is possible, but varicella–zoster virus is labile and relatively difficult to recover from swabs of cutaneous lesions. A direct immunofluorescence assay is more sensitive than viral culture and has the additional advantages of a lower cost and a more rapid turnaround time. Like culture, the direct immunofluorescence assay can distinguish herpes simplex virus infections from varicella–zoster virus infections. Polymerase-chain-reaction techniques are useful for detecting varicella–zoster virus DNA in fluid and tissues. For the purposes of this study, due to financial and time constraints and unavailablility of some of the diagnostic techniques, diagnosis will be determined clinically by an experienced dermatologist.

Dahl H, Marcoccia J, Linde A. Antigen detection: the method of choice in comparison with virus isolation and serology for laboratory diagnosis of herpes zoster in human immunodeficiency virus-infected patient. *J Clin Microbiol* 1997;35:345-9.

CUTANEOUS TUBERCULOSIS:

Conventional investigations such as cultures and acid-fast bacillus (AFB) smears for the diagnosis of cutaneous tuberculosis have many inherent limitations. Detection rate of AFB in cutaneous TB, which is a paucibacillary form of the disease, is very low. Recovery of the bacilli either in artificial medium and/or in guinea pigs requires at least 6 to 8 weeks; moreover, a positive culture is not always obtained. Therefore, the clinical diagnosis of skin TB in a large number of patients is supported by histopathology.

Sehgal VN, Bhattacharya SN, Jain S, Logani K. Cutaneous tuberculosis: the evolving scenario. *Int J Dermatol* 1994; **33**: 97–104.

KAPOSI'S SARCOMA:

The diagnosis of KS in the skin and mucous membranes can usually be made based on the following clinical features:

1. Purple macules or nodules
2. Distribution along skin tension lines
3. Green-yellow discoloration around the tumors corresponding to hemorrhage
4. Surrounding edema
5. Dissemination of lesions, possibly with mucocutaneous involvement

This is particularly characteristic for patients in whom HIV infection or another form of immunodeficiency is known. If there is clinical doubt, the lesions should be biopsied to confirm the diagnosis histologically. The clinical presentation may pose a challenge, especially with the telangiectatic, ecchymotic, keloidal and hyperkeratotic variants.

Tappero JW, Conant MA, Wolfe SF, et al. Kaposi's sarcoma: epidemiology, pathogenesis, histology, clinical spectrum, staging criteria and therapy. *J Am Acad Dermatol* 1993, 28: 371-95.

SCABIES:

A presumptive diagnosis can be made, based on a typical history of pruritis, worse at night, and the distribution of the inflammatory papules. A supportive history of contact with other cases can be frequently obtained. Parasitological confirmation of the diagnosis can be most easily obtained by gently scraping the skin off the burrow with a blunt scalpel blade, and placing the material on a glass slide with a drop of 10% potassium hydroxide or mineral oil, and seeking mites, eggs, or eggshells by low power microscopy.

Hogan DJ, Schachner L, Tanglertsampan C. Diagnosis and treatment of childhood scabies and pediculosis. *Pediatr Clin North Am* 1991;38:941–57.

APPENDIX V:

GUIDELINES FOR SKIN BIOPSY:

INDICATIONS:

- Suspected neoplastic lesions.
- To confirm a clinical diagnosis (see appendix VIII)
- Atypical lesions (see appendix VIII)

CONTRAINDICATIONS:

- An infected site.
- Patients with bleeding disorders.
- Skin lesions in areas such as the face for cosmetic purposes
- Skin lesions in areas with poor healing eg distal lower extremities
- Cartilaginous areas like the ear, nose etc.
- Severe immunosuppression or severely ill patient.
- Secondary lesions.

APPENDIX VI:

LABORATORY DIAGNOSIS OF RINGWORM:

COLLECTION OF SPECIMENS:

1. Cleanse the affected area with 70% ethanol
2. Collect skin scales, crusts, pieces of nail, or hairs on a clean piece of paper as follows:
   - Skin scales: collect by scraping the surface of the margin of the lesion using a sterile scalpel blade.
   - Crusts: collect by removing part the crust nearest to healthy using sterile scissors and tweezers.
   - Nail pieces: collect by taking snippings of the infected part of the nail using sterile scissors.
   - Hairs: collect by removing dull broken hairs from the margin of the lesion using tweezers.
3. After collecting the specimens, fold the paper to form a flat packet. Label with the patient's name and number, source of material, and the date collected.
4. Close the packet with a paper clip (do not use a staple). Wash hands with soap and water after handling specimens.

)IRECT MICROSCOPY:

.. Place a drop of potassium hydroxide (KOH) solution on a slide.

. Transfer the specimen (small pieces) to the drop of KOH, and cover with a cover glass. Place the slide of in a petri dish, or other container with a lid, together with a damp piece of filter paper or cotton wool to prevent the preparation from drying out.

. As soon as the specimen has cleared, examine it microscopically using the 10x and 40x objectives with the condenser iris diaphragm closed sufficiently to give good contrast.

APPENDIX VII:

TERMINOLOGY IN DERMATOLOGY:

Lesion A lesion is any single area of altered skin. It may be solitary or multiple.
Rash A rash is a widespread eruption of lesions.
Dermatosis Dermatosis is another name for for skin disease.

Distribution:

Distribution refers to how the skin lesions are scattered or spread out. Skin lesions may be isolated (solitary or single) or multiple. The localisation of multiple lesions in certain regions helps diagnosis, as skin diseases tend to have characteristic distributions. What is the extent of the eruption and its pattern?

- **Acral** Affects distal portions of limbs (hand, foot) and head (ears, nose).
- **Blaschko's lines** Following a roughly linear, segmental pattern described by Blaschko and thought to be indicative of somatic mosaicism.
- **Dermatomal** Corresponding with nerve root distribution.
- **Extensor** Involving extensor surfaces of limbs. Contrast with **flexor** surfaces.
- **Flexural** Involving skin flexures (body folds); also known as **intertriginous**.
- **Follicular** Individual lesions arise from hair follicles. These may be grouped into confluent plaques.
- **Generalised** Universal distribution: may be mild or severe, **scattered** or **diffuse**
- **Herpetiform** Grouped umbilicated vesicles, as arise in *Herpes simplex* and *Herpes zoster* infections.
- **Koebnerised** Arising in a wound or scar. The Koebner phenomenon refers to the tendency of several skin conditions to affect areas subjected to injury.
- **Photosensitive**
  Favouring sun exposed areas. Does not affect skin that is always covered by clothing.
  - Head & neck: spares eyelids, depth of wrinkles & furrows, areas shadowed by hair, nose & chin. Typically involves V of neck.
  - Backs of hands: spares finger webs. More severe on proximal than distal phalanges.
  - Forearms: extensor rather than flexor.
  - Feet: dorsal surface, sparing areas covered by footwear.
  - Lower legs: may affect extensor and/or flexor surfaces
  - Trunk: rarely affected
- **Pressure areas**
  Affecting areas regularly prone to injury from pressure at rest.
  - Tops of the ears when sleeping
  - Buttocks when sitting
  - Heels when lying
- **Seborrhoeic**
  The areas generally affected by seborrhoeic dermatitis, with a tendency to oily skin (seborrhoea). Scalp, behind ears, eyebrows, nasolabial folds, sternum and interscapular.
- **Symmetrical** In the same regions, the left side is affected in a similar way to the right side.
- **Truncal** Favours trunk and rarely affects limbs.
- **Unilateral** Wholly or predominantly on one side of the affected region.

Configuration of Lesions:

Configuration refers to the shape or outline of the skin lesions. Skin lesions are often grouped together. The pattern or shape may help in diagnosis as many skin conditions have characteristic configuration.

- **Nummular lesion** Round (coin-shaped) lesions. Also known as **discoid**.
- **Linear lesion** A linear shape to a lesion often occurs for some external reason such as scratching. Also **striate**.
- **Target lesion** Concentric rings like a dartboard. Also known as **iris** lesion.
- **Gyrate rash** A rash that appears to be whirling in a circle.
- **Annular** Lesions grouped in a circle.

Colour:

Descriptive terms used to describe skin colour include:

- **Carotenaemia** Excessive circulating beta-carotene (vitamin a precursor derived from yellow/orange coloured vegetables and fruit) results in yellow/orange skin colouration. Tends to be pronounced on palms and soles. Does not affect cornea.
- **Hyperpigmentation** Hypermelanosis or haemosiderin deposits result in skin colour that is darker than normal.
- **Hypopigmentation** Loss of melanin results in skin colour that is paler than normal but not completely white.
- **Leukoderma** White skin. Also known as **achromia**.
- **Infarcts** Infarcts are black areas of necrotic tissue due to interrupted blood supply.
- **Jaundice** Excessive circulating bilirubin results in yellow/green skin colour, prominent in cornea.
- **Erythema** Localised area of red skin due to increased blood supply and blanch with pressure (diascopy).
- **Erythroderma** The skin condition affects the whole body or nearly the whole body, which is red all over.
- **Telangiectasia** Telangiectasia is the name given to prominent cutaneous blood vessels.
- **Purpura** Purpura is bleeding into the skin. This may be as **petechiae** (small red, purple or brown spots) or **ecchymoses** (bruises). Purpura does not blanch with pressure (diascopy).

Morphology:

Morphology is the form or structure of an individual skin lesion.

- Skin lesions may be **flat**, **elevated** above the plane of the skin or **depressed** below the plane of the skin.
- They may be **skin coloured** or **red, pink, violaceous, brown, black, grey, blue, orange, yellow**.
- Consistency may be **soft**, **firm**, **hard**, **fluctuant** or **sclerosed** (scarred or board-like).
- The lesions may be **hotter** or **cooler** than surrounding skin.
- They may be **mobile** or **immobile**.

Macule A macule is an area of colour change less than 1.5 cm diameter.
The surface is **smooth**.
Patch A patch refers to a large area of colour change, with smooth surface.
Papule Papules are small palpable lesions. The usual definition is that they are less than 0.5 cm diameter, although some authors allow up to 1.5 cm. They are raised above the skin surface, and may be **solitary** or **multiple**.

Papules may be:

- **Acuminate** (pointed)
- **Dome-shaped** (rounded)
- **Filiform** (thread-like)
- **Flat-topped**
- **Oval** or **round**
- **Pedunculated** (with a stalk)
- **Sessile** (without a stalk)
- **Umbilicated** (with a central depression)
- **Verrucous** (warty)

A **nodule** is an enlargement of a papule in three dimensions (height, width, length). It is a solid lesion.
A **cyst** is a papule or nodule that contains fluid so is fluctuant.
A **plaque** is a palpable flat lesion greater than 0.5 cm diameter. Most plaques are elevated, but a plaque can also be a thickened area without being visibly raised above the skin surface. They may have well-defined or ill-defined borders.
Plaques may be:

- **Annular** (ring shaped)
- **Arcuate** (half-moon)
- **Polygonal** (varied non-geometric shape)
- **Polymorphic** (varied shape)
- **Serpiginous** (in the shape of a snake)
- **Poikilodermatous** (variegated appearance, usually mixed pallor, telangiectasia & pigmentation)

Vesicle Vesicles are small fluid-filled blisters less than 0.5cm diameter. They may be single or multiple.
Pustule A pustule is a purulent vesicle. It is filled with neutrophils, and may be white, or yellow. Not all pustules are infected.
Bulla A bulla is a large fluid-filled blister. It may be a single compartment or multiloculated.
Abscess An abscess is a localised collection of pus.
Weal A wheal is an oedematous papule or plaque caused by swelling in the dermis. Wealing often indicates urticaria.

Skin surface:

The skin surface of a skin lesion may be normal or smooth because the pathological process is below the surface, either dermal or subcutaneous. Surface changes indicate epidermal changes are present.
Scaling or **hyperkeratosis**is an increase in the dead cells on the surface of the skin (stratum corneum).
Descriptive terms for scale include:

- **Desquamation** (skin coming off in scales)
- **Psoriasiform** (large white or silver flakes)
- **Pityriasiform** (branny powdery scale)
- **Lichenoid** (apparent scale is tightly adherent to skin surface)
- **Keratotic** (horny scale)
- **Exfoliation** (peeling skin)
- **Maceration** (moist peeling skin)
- **Verrucous** (warty)

Secondary changes:
Lichenification
Lichenification is caused by chronic rubbing, which results in palpably thickened skin with increased skin markings and lichenoid scale. It occurs in chronic atopic eczema and lichen simplex.

Crusting Crust occurs when plasma exudes through an eroded epidermis. It is rough on the surface and is yellow or brown in colour. Bloody crust appears red, purple or black.
Dystrophy Dystrophy refers to degeneration or abnormal formation of the skin. It is often used to refer to nail diseases.
Excoriation An excoriation is a scratch mark. It may be linear or a picked scratch (**prurigo**). Excoriations may occur in the absence of a primary dermatosis.
Erosion Erosion is caused by loss of the surface of a skin lesion; it is a shallow moist or crusted lesion.
Fissure A fissure is a thin crack within epidermis or epithelium, and is due to excessive dryness.
Fungating Refers to a large malignant tumour that is erupting like a mushroom or fungus.
Granulation tissue Granulation tissue is a made of a mass of new capillaries and fibrous tissue in a healing wound.
Ulcer An ulcer is full thickness loss of epidermis or epithelium. It may be covered with a dark-coloured crust called an **eschar**.
Granuloma A granuloma is a histological (pathological) term refering to chronic inflammation in which there are several types of inflammatory cells including giant cells. Granulomas form in response to foreign bodies, certain infections (tuberculosis, leprosy) and inflammatory skin diseases (granuloma annulare, granuloma faciale, sarcoidosis).
Hypertrophy Some component of the skin such as a scar is enlarged or has grown excessively. The opposite is **atrophy** or thinned skin.

APPENDIX VIII: PHOTOALBUM

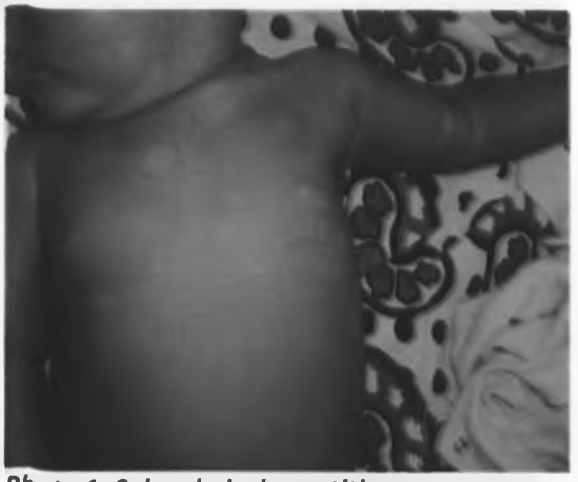


Photo 1: Seborrheic dermatitis

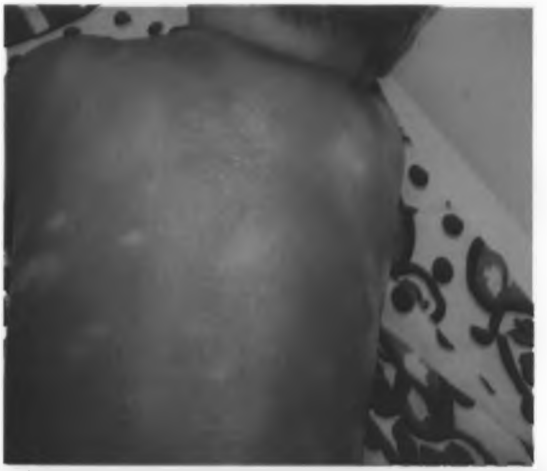


Photo 2: Seborrheic dermatitis

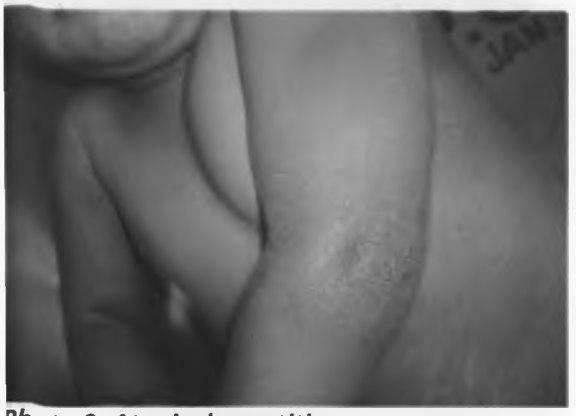


Photo 3: Atopic dermatitis

Photo 4: Atopic dermatitis

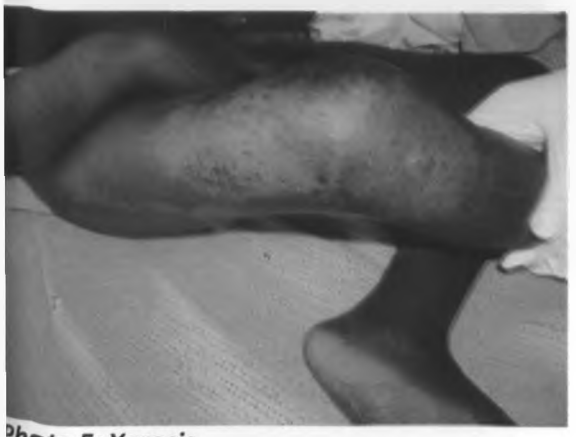


Photo 5: Xerosis

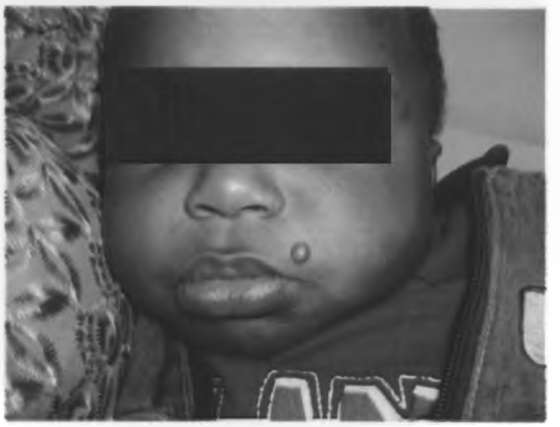
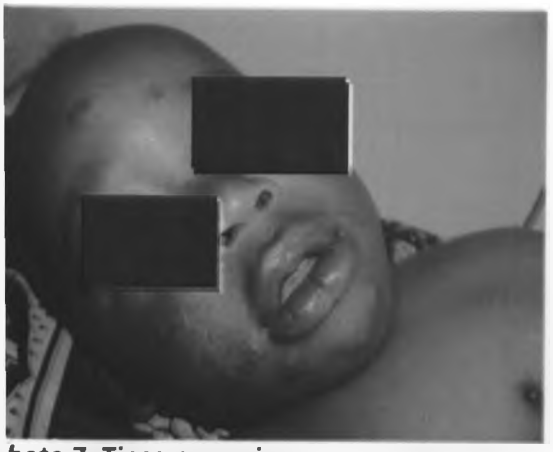


Photo 6: Molluscum contagiosum



hoto 7: Tinea corporis

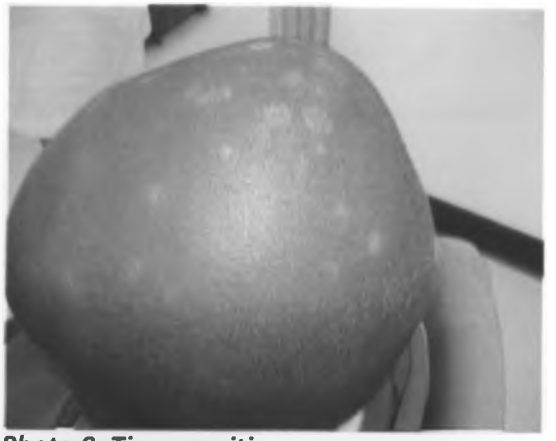
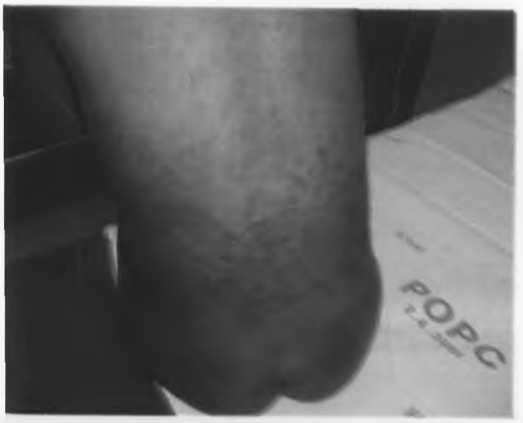


Photo 8: Tinea capitis



ıoto 9: Papular urticaria

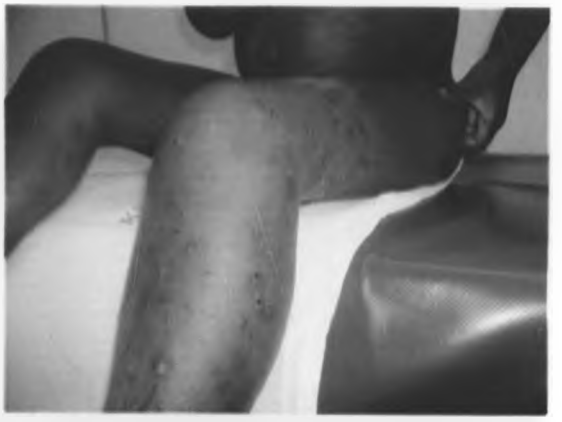
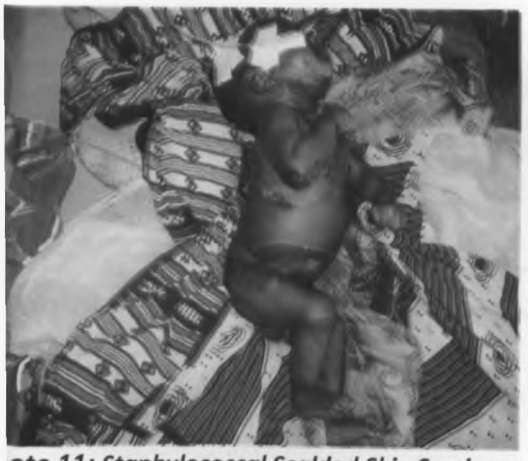


Photo 10: Papular urticaria



oto 11: Staphylococcal Scalded Skin Syndrome

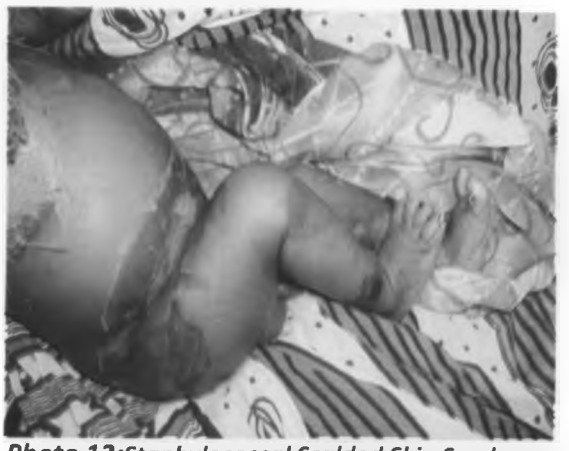


Photo 12:Staphylococcal Scalded Skin Syndrome

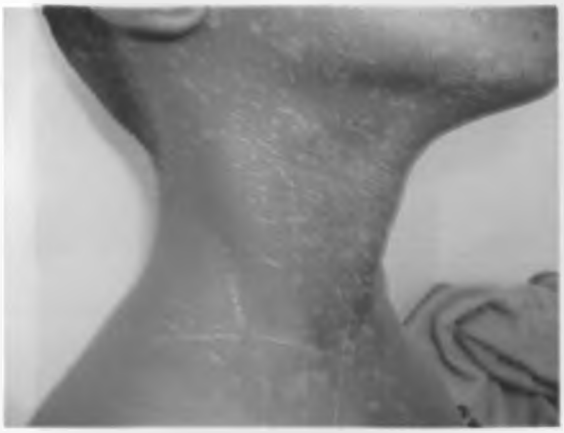


Photo 13: Verrucae plana

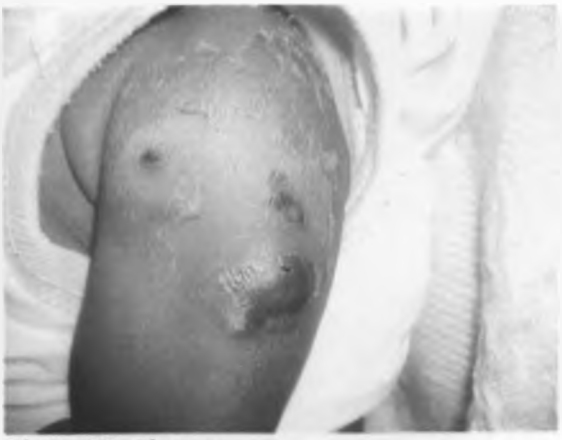


Photo 14: Abscess

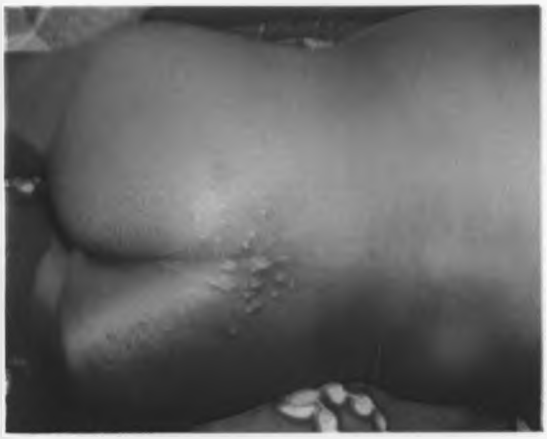


Photo 15: Folliculitis

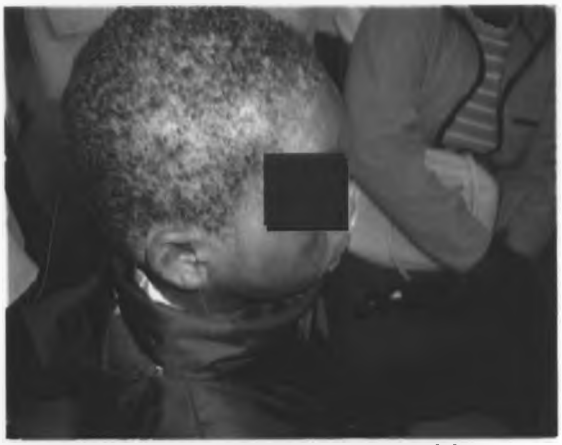


Photo 16: Irritant Contact Dermatitis

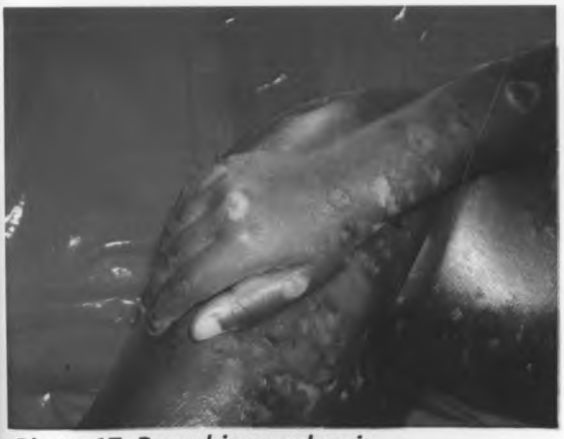


Photo 17: Pemphigus vulgaris

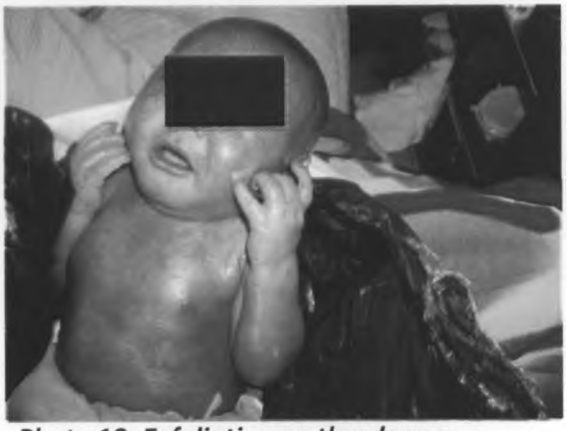


Photo 18: Exfoliative erythroderma

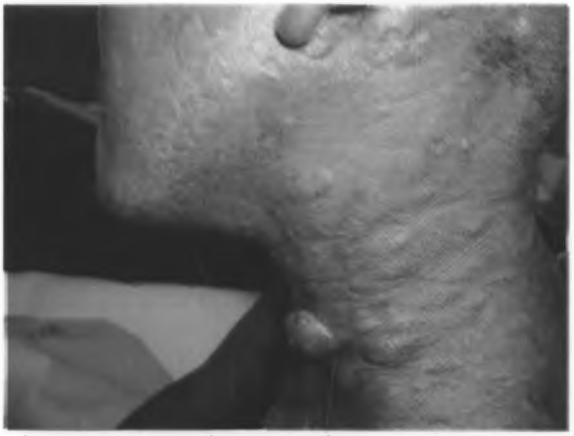


Photo 19: Mycosis Fungoides

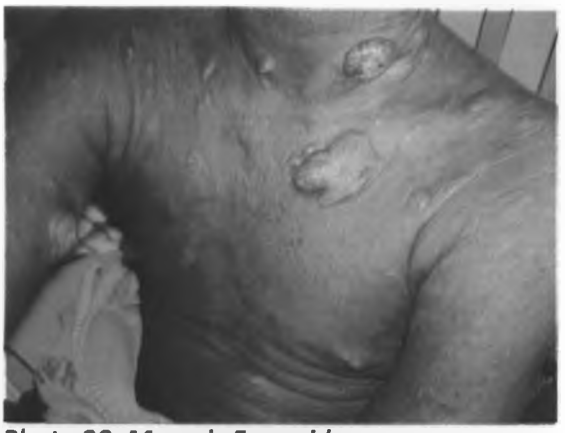


Photo 20: Mycosis Fungoides