SKIN( & mucocutaneous) MANIFESTATIONS OF HIV

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PRESENTATION OBJECTIVES

• To introduce common muco-cutaneous manifestations of HIV disease

• To raise the index of suspicion for HIV in the HCW confronted by a patient presenting with a skin disease by highlighting “red-flag skin conditions”

• To contribute to a reduction in the stigma and discrimination that patients with skin disease encounter
In 1981 the era of HIV disease was heralded by the paper: Hymes, K B et al - Kaposi’s sarcoma in homosexual men: A report of 8 cases Lancet 2 : 598-600

Kaposi’s sarcoma was thus recognized as the first cutaneous marker of HIV infection

Retrieved from www.sciencephoto.com
http://www.sciencephoto.com/media/251567/view
• From the beginning, skin disease played a prominent role in
  the identification of the emerging pandemic
  as well as identifying individuals infected with HIV
• Cutaneous disease not only marked the presence of this acquired impaired cellular immunity but also its severity
Pathophysiology of Skin disease in HIV

“TYPE 1”
- CYTOKINES
  - IL2
  - TNF-α
  - IFN-γ

→ PSORIASIS

“TYPE 2”
- CYTOKINES
  - IL4
  - IL5
  - IL6
  - IL10

HIV

Source: Dermatol Online J © 2007 Arthur C. Huntley, MD
New insights into HIV-1-primary skin disorders
Filiberto Cedeno-Laurent, Minerva Gómez-Flores, Nora Mendez, Jesús Añer-Rodríguez, Joseph L Bryant, Anthony A Gaspar and Jose R Trujillo*
Box 21.6 Mucocutaneous disorders stratified by CD4 count

<table>
<thead>
<tr>
<th>CD4 range (per µL)</th>
<th>Skin diseases</th>
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<tbody>
<tr>
<td>&gt;500</td>
<td>• Acute retroviral syndrome</td>
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<tr>
<td></td>
<td>• Oral hairy leukoplakia</td>
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<tr>
<td></td>
<td>• Vaginal candidiasis</td>
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<td></td>
<td>• Seborrheic dermatitis</td>
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<td></td>
<td>• Psoriasis</td>
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<td></td>
<td>• Kaposi’s sarcoma</td>
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<tr>
<td>200-500</td>
<td>• Oral thrush</td>
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<td></td>
<td>• Herpes zoster</td>
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<td>• Herpes simplex</td>
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<td></td>
<td>• Refractory psoriasis</td>
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<td></td>
<td>• Hypersensitivity to nevirapine</td>
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<td></td>
<td>• Condyloma acuminatum</td>
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<td></td>
<td>• Tinea infection</td>
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<td></td>
<td>• Verruca vulgaris</td>
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<tr>
<td>100-200</td>
<td>• Disseminated herpes simplex</td>
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<td></td>
<td>• Refractory seborrheic dermatitis</td>
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<td></td>
<td>• Eosinophilic folliculitis</td>
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<td></td>
<td>• Pruritic papular eruption</td>
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<td></td>
<td>• Molluscum contagiosum</td>
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<tr>
<td></td>
<td>• Extensive Kaposi’s sarcoma</td>
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<tr>
<td>&lt;100</td>
<td>• Cutaneous pemphigoid</td>
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<tr>
<td></td>
<td>• Basaloid angiomatosis</td>
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<tr>
<td></td>
<td>• Herpes simplex: large &amp; unhealing</td>
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<td></td>
<td>• Cutaneous cryptococcus</td>
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<td></td>
<td>• Giant mollusca</td>
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<td></td>
<td>• Disseminated alphogroupalovirus</td>
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<tr>
<td></td>
<td>• Acquired ichthyosis</td>
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</tbody>
</table>
WHO Clinical Staging System

Clinical Stage 1
- Asymptomatic infection
- Persistent generalized lymphadenopathy (PGL)
- Acute retroviral infection

Clinical Stage 2
- Unintentional weight loss, < 10%
- Minor mucocutaneous manifestations
- Herpes zoster, within previous 5 years
- Recurrent upper respiratory tract infections
WHO Clinical Staging System

Clinical Stage 3

- Unintentional weight loss, >10%
- Chronic diarrhea
- Prolonged fever
- Oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis
- Severe bacterial infections
- Vulvovaginal candidiasis
WHO Clinical Staging System

Clinical Stage 4

16. HIV wasting syndrome
17. PCP
18. Toxoplasma of the brain
19. Cryptosporidiosis with diarrhea
20. Isosporiasis with diarrhea
21. Extrapulmonary cryptococcosis
22. Cytomegaloviral disease of an organ other than liver, spleen, or lymph node
23. Herpes simplex virus infection
24. PML (progressive multifocal leukoencephalopathy)
25. Any disseminated endemic mycosis
26. Candidiasis of the esophagus, trachea, bronchi, and lungs
27. Atypical mycobacteriosis
28. Non-typhoid Salmonella septicemia
29. Extrapulmonary TB
30. Lymphoma
31. Kaposi’s sarcoma
32. HIV encephalopathy
Characteristics of HIV/AIDS Dermatology

- Multiple skin conditions occurring in one patient
- Unusual presentations of common conditions
- Conditions may be difficult to recognize
- Conditions may be recalcitrant to treatment
A skin disease may be the first sign of HIV infection.
The prevalence of mucocutaneous disorders among HIV-positive patients attending an out-patient clinic in Kingston, Jamaica

DS Thompson, B Bain, A East-Innis
West Indian Medical Journal Jan 2008

• 286 patients
• 74% had a mucocutaneous disorder
<table>
<thead>
<tr>
<th>Skin disorder</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Papular prurigo</td>
<td>32</td>
</tr>
<tr>
<td>Oral candida</td>
<td>29</td>
</tr>
<tr>
<td>Dermatophyte infection</td>
<td>11</td>
</tr>
<tr>
<td>Herpes genitale</td>
<td>8</td>
</tr>
<tr>
<td>Eosinophilic folliculitis</td>
<td>8</td>
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<tr>
<td>Seborrhoeic eczema</td>
<td>7</td>
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</tbody>
</table>
RED FLAG CONDITIONS

“Skin conditions that should raise the index of suspicion for HIV infection”
PAPULAR & PRURITIC

Images retrieved from-
Pruritic Papular Eruption (PPE)

- Diffuse pruritic eruption occurring in HIV infected patients
- Primary lesion is a firm, discrete, hyperpigmented/erythematous, urticarial papule/plaque
- Occurs mostly on the extremities, but trunk and face involved in 50% of cases

Image retrieved from
http://www.ncbi.nlm.nih.gov/pmc/tools/ope
nftlist/
Photos from Web study
• Excoriated papules and marked post-inflammatory hyperpigmentation occurs

• Scarred nodules

Photo from Web study
Papular Pruritic Eruption

- It is less common in immunocompetent patients
- More than 50% of HIV infected patients in some countries report the eruption as their initial disease manifestation
- Reported positive predictive value of 82-87% for HIV

PPE PATHOGENESIS

Resneck et al  JAMA December 1, 2004 – Vol 292, 21

- PPE in HIV – infected individuals may be a reaction to arthropod bites
- Represents an altered and exaggerated immune response to arthropod antigens
Images retrieved from UW Web study
Eosinophilic folliculitis (E.F.) of HIV

- Has a characteristic morphology and distribution
- Always itchy
- Common in advanced stages of HIV without therapy
- Becoming more commonly recognized after initiation of ART with immune reconstitution.*

Eosinophilic folliculitis

- Chronic, intensely pruritic condition
- Pathogenesis & etiology not explained - Immune response to an unknown antigen or OI (fungi, yeasts, demodex mites implicated)
- Clinically – 2-3 mm erythematous oedematous folliculocentric papules, less commonly pustules on forehead, neck, shoulders, trunk and upper arms
- Occurs in advanced disease  CD4 < 75 – an important cutaneous marker of late stage disease
Photos courtesy Dr C Anderson
Seborrheic dermatitis

- Affects 4% of the general population and 85% of HIV positive population
- Yellow-white greasy scales on erythematous patches affecting sebaceous areas – face, scalp, chest, back and intertrigenous areas
- In HIV positive individuals the scalp involvement may be particularly severe
- In some patients a generalized erythroderma involving trunk and extremities may occur
Seborrheic Dermatitis - infected

Photos courtesy Dr C Anderson
- annular seborrheic dermatitis, also called petaloid seborrheic dermatitis or seborrhea petaloides.

- Sarcoidosis, secondary syphilis, and even discoid lupus should be in the differential in such cases.
Seborrheic dermatitis

- May occur at any CD4 cell count
- Extent, abruptness of onset, distribution, severity increases with reduced CD4
- Response to treatment tends to be more difficult as the CD4 deteriorates
Diffuse xerosis & acquired ichthyosis was found to be closely correlated with more advanced phases of AIDS - Rosatelli et al Int J of Derm 1997, 36, 729-734
XEROSIS

• Suggested pathogenesis:

✓ Changes in microcirculation
✓ Decreased sweat, oils on skin
✓ Deranged nutrient supply
✓ Decreased innervation of skin
CRUSTED SCABIES - DO NOT SHAKE THIS HAND

Images retrieved from http://www.pic2fly.com/Norwegian+Scabies.html
Photo from UW Web study
MOLLUSCUM CONTAGIOSUM

Images retrieved from http://www.pic2fly.com
Molluscum contagiosum

RED FLAG
Occurring on face
Larger lesions than usual
More numerous
Molluscum contagiosum

- Benign viral disease of the skin
- Poxvirus - transmitted by direct contact or by infected fomites
- May be sexually transmitted
- Incubation period of 2-7 weeks, latency of up to 6 months
- Greatest incidence in children < 5 yrs

Molluscum contagiosum

- Cutaneous viral infection manifested as 2-3 mm flesh coloured papules hemispheric papules
- Characteristically a faint whitish core at the centre of each papule, some may be slightly umbilicated
- Common in immunocompetent children (3-6yrs) with lesions scattered over face, arms and trunk. Lesions resolve spontaneously in 6-12 months
- In adults the infection is sexually transmitted and may be chronic
Molluscum contagiosum in HIV

- Molluscum contagiosum occurs in 10-20% of HIV infected persons
- Early in the infection the lesions are mild and localized on the groin, neck or face
- Once the CD4 falls below 200 - lesions tend to proliferate, and involve the face, trunk, groin
- **Extensive Molluscum contagiosum is a cutaneous marker of advanced HIV disease (CD4< 50)**
Treatment of Molluscum contagiosum

• Objective of treatment is primarily cosmetic – no known medical complications, it does not affect internal organs or cause significant skin symptoms

• Most important component of therapy is to improve the patients immune status with ART
DEMATOPHYTE INFECTIONS

EXTENSIVE TINEA CORPORIS

Photo courtesy Dr C Anderson
• Considered an early marker of HIV infection.

The fungus invades through the proximal nail fold at the cuticle area, penetrates the newly formed nail plate, proceeds distally, and eventually penetrates all nail layers and the entire nail.

The end result is total dystrophic onychomycosis with a convex, irregular, and rough nail.
RED FLAG
Multidermatomal Zoster

HIVc 19
Varicella Zoster virus (VZV) infection

- VZV infection is commonly seen early in the course of HIV infection, before the onset of other symptoms
- The initial presentation is usually herpes zoster/shingles
- Herpes zoster often precedes thrush and oral hairy leukoplakia by about 1 year
- Incidence of zoster among HIV infected adults is more than 10-fold that of age matched immunocompetent persons
- **Important early finding and should raise suspicion of HIV infection in persons at risk**
Herpes Zoster in HIV

- Eruption may be bullous, hemorrhagic, necrotic and particularly painful
- Blisters and crusts last longer – 2-3 weeks
- Necrotic lesions may last up to 6 weeks and heal with severe scarring
- Recurrences are common – 25% of African HIV infected persons
- Chronic disseminated VZV may present as widespread ulcers or hyperkeratotic verrucous lesions
ZOSTER SCARRING

Photos from e-TALC
HERPES ZOSTER – complications

- Hutchinsons sign - Involvement of the tip of the nose from herpes zoster, a sign taken to indicate that the eye may be seriously involved by VZV because of the involvement of the nasal branch of the nasociliary nerve.

Image retrieved from - http://kootation.com/what-is-herpes-therapy-for-you.html
Patient complains of sore mouth, food tastes funny

Thrush on hard and soft palate. Note that erythema is almost absent

Oral thrush involving hard and soft palate
Angular cheilitis

Image retrieved from – IARC website
http://screening.iarc.fr/atlas
ATROPHIC CANDIDA

• **chronic atrophic candidiasis** - Central papillary atrophy of the tongue. Note the papillary atrophy in the mid part of *dorsum tongue* with multiple lobular and fissured appearance.

• The symptomatology in this variety is less intense than in acute pseudomembranous candidiasis. Patients mostly complain of a burning sensation.
Oropharyngeal candida

- Most common cause of dysphagia in the HIV patient
- Treat with azoles:
  - Fluconazole 100-200mg od 14-21 days
  - Nystatin suspension 4-6ml gargle 6 hourly
Oral leukoplakia
Oral hairy leukoplakia

- Proliferative changes of the papilla on the tongue
- Most often on the lateral borders of the tongue but also on ventral and dorsal surfaces of the tongue, the buccal mucosa and palate
- EB virus detected by immunochemistry
- Usually not treated - High dose acyclovir & Podophyllin resin have been tried
- Recurrences common
ANOGENITAL Lesions

Images retrieved from sciencephotolibrary
Herpes simplex virus infection

- Atypical chronic ulcers
- Occur with advanced immunosuppression (CD4 < 100)
- Presence of chronic ulcerative HSV lesions for at least 1 month – AIDS defining condition
HIV and the Skin: Parting Advice

- Look at the entire skin, not just what the patient shows you.
- Don’t forget syphilis, HSV, and scabies!
- Biopsy, culture and scrape that which you aren’t sure about.
- Seek help when you need it.
Conclusion

- The skin is the most common organ affected in HIV disease. 90% of HIV-infected individuals will present with skin disease during the course of the infection.

- The skin barrier is the first to be disrupted and often is the sentinel sign of HIV infection.
  Viral, bacterial and fungal infections in addition to inflammatory disorders have all been reported to increase as CD4 cells are depleted.

- Certain skin disorders are so closely related to immune status that their appearance is considered stage defining.
THANK YOU

"Here, don’t touch the stick."
Papular Pruritic eruption

Unfortunately pruritic papular eruption of HIV often proves very resistant to treatment. However, there are a number of different treatment approaches that have been shown to be effective in at least some patients.

- Topical steroid, emollients and oral antihistamines should be the first line approach, because of their availability and safety.
- Failing this phototherapy (UVB or PUVA) should be commenced. This is usually effective. The average time for the skin condition to recur is 8 weeks.
- Another reported useful agent is pentoxifilline. This is thought to be work by its TNFα inhibitor effect. The usual dose is 400mg three times daily for at least 8 weeks.
- Whether HAART (Highly Active Anti-Retroviral Therapy) makes a difference is debated and the response is variable. But because some people have seen consistent responses, there has been a recommendation that pruritic papular eruption is used as qualification for initiating HAART.
Eosinophillic folliculitis - treatment

- Itraconazole 200mg daily (Fluconazole not helpful)
- Oral isotretinoin 40-80mg/day for 1-4 weeks
- Antihistamines – cetrizine
- Metronidazole 250-500mg bd x 3-4 weeks
- Suppression – tretinoin topically decreases the rate of appearance of new lesions but does not affect established ones

- EF responds favorably to HAART – do not stop ART
Seborrheic dermatitis - treatment

- Therapeutic shampoos – ketoconazole, zinc pyrithione, tar
- Topical therapy – steroids, sulphur, salicylic acid mixtures, ketoconazole cream
- UVB therapy
Treatment of Molluscum Contagiosum

- Self limiting disorder
- Cryosurgery
- Evisceration
- Light electrodessication & curettage
- Tretinoin 0.1% cream bd
- Cimetidine 40 mg/kg/day in two divided doses for 2 months
- Pulsed dye laser
- Imiquimod 5% cream nightly
• Permethrin
• Benzyl benzoate
• Lindane
• Others
Herpes Zoster - treatment

- Acyclovir reduces pain, speeds healing and reduces risk of dissemination
- Initiate as soon as possible – within 3 days
- Dosage 800mg orally 5 times daily for 5 days, continue for 5 days beyond last day of blister formation
- Intravenous acyclovir (10mg/kg 3 times daily) is indicated with significant immunosuppression - CD4 < 200, for disseminated lesions or when VZV affects the optic branch of the trigeminal nerve
Treatment of HSV infection

- Moderate to severe lesions usually require 14 days
- Continue therapy until lesions are healed
- Consider suppressive therapy for patients with frequent or severe recurrences – HSV outbreaks may result in increased HIV transcription and increased plasma HIV RNA levels
BASIC SKIN CARE

- Bathe in cool water
- Use pH neutral syndet (non soap) bars
- Do not use medicated or highly perfumed soaps
- Pat skin dry – do not rub
- Apply good moisturizer within 2-3 mins
- Good moisturizer – water in oil
- Repeat moisturizer 6-8 x day
- Apply perfumes to clothing not skin -if at all
- Use a sun block
- Avoid frequent use of oily products on the scalp