Oral Manifestations of Sexually Transmitted Infections

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The first cases of what would later be known as HIV/AIDS – June 5, 1981

Adults and children estimated to be living with HIV | 2012

Diagnoses of HIV Infection among Adults and Adolescents, by Transmission Category, 2011—United States and 6 Dependent Areas

<table>
<thead>
<tr>
<th>Transmission Category</th>
<th>No.</th>
<th>%</th>
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<tbody>
<tr>
<td>Male-to-male sexual contact</td>
<td>30,896</td>
<td>61.8</td>
</tr>
<tr>
<td>Injection drug use (IDU)</td>
<td>3,836</td>
<td>7.7</td>
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<tr>
<td>Male-to-male sexual contact and IDU</td>
<td>1,423</td>
<td>2.9</td>
</tr>
<tr>
<td>Heterosexual contact*</td>
<td>13,801</td>
<td>27.6</td>
</tr>
<tr>
<td>Otherb</td>
<td>51</td>
<td>0.1</td>
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<tr>
<td>Total</td>
<td>50,007</td>
<td>100.0</td>
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Note: Data includes persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data is based on 2011 estimates. The total number of diagnoses includes persons in both heterosexual and non-heterosexual transmission modes. It includes all persons with a diagnosis of infection regardless of transmission mode.
Interactive Maps – AIDSvu.org

- National, State, and Local Maps
  - Persons living with an HIV diagnosis by state, county, ZIP code and census tract
  - Social determinants of health (e.g., poverty, lack of health insurance, educational attainment)
  - HIV transmission modes
  - HIV testing and treatment center locations
  - NIH-funded HIV Prevention, Vaccine & Treatment Trials Sites

Oral Manifestations of HIV Disease: The Basics

- Oral manifestations of HIV infection are a fundamental component of disease progression.
- There has been a significant decrease in the overall prevalence of oral lesions from 47 – 85% pre-cART to 32-46% post cART.
- Factors, which predispose expression of oral lesions, include:
  - CD4 counts less than 200 cells/mm^3
  - Viral load greater than 3,000 copies/mL
  - Xerostomia (dry mouth)
  - Poor oral hygiene
  - Smoking

Trends in Oral Manifestations

- Studies from both the Americas and Europe report a decreased frequency of HIV-related oral manifestations of 10-50% following the introduction of ART.
- Evidence suggests that cART plays an important role in controlling the occurrence of oral candidiasis.
- The effect of cART on reducing the incidence of oral lesions, other than oral candidiasis, does not appear as significant.
Trends in Oral Manifestations
Advances in Dental Research 04/06
Hodgson TA, Greenspan D, Greenspan JS

- Increased prevalence of oral warts in patients on cART has been reported from the USA and the UK.
- HIV-related salivary gland disease may show a trend of rising prevalence in the USA and Europe.
- A possible association between an increased risk of oral squamous cell carcinoma and HIV infection has been suggested by at least three epidemiological studies.


- A retrospective study based on chart review was conducted among patients (n = 744) who were ≥19 years of age and initiated cART between 01/2000 and 06/06 at the University of Alabama at Birmingham (UAB) 1917 Clinic.
- Patients’ laboratory data and oral conditions were recorded for 2 years after enrollment into the study.
- During 2 years of follow-up 35.6% (266/744) experienced at least one oral lesion.

Oral Manifestations of HIV/AIDS

- For those with unknown HIV status, oral manifestations may suggest HIV infection, although they are not diagnostic.

- Oropharyngeal candidiasis (OPC) was the most frequent manifestation.
- Patients undergoing cART continue to be affected by HIV-related oral conditions, especially OPC.
- These results clearly indicate that oral lesions during HIV infection are still highly prevalent in spite of the improvements in medical care and the availability of cART.

Oral Manifestations of HIV/AIDS

For persons living with HIV disease not yet on therapy, the presence of certain oral manifestations may signal progression of disease.


Oral Manifestations of HIV/AIDS

For persons living with HIV disease on antiretroviral therapy the presence of certain oral manifestations may signal a failure in therapy.

Case Study #1

- 42 year old African-American female presented to the Oral Health Center for routine restorative dental work 02/04/07. She was originally diagnosed in 1999 with a CD4 count of 13 cells/mm³. Reports health is within normal limits, no new symptoms.
- Against her providers recommendations, she stopped taking her antiretroviral therapy in the latter part of November 2006.
- Her last CD4 count, taken early November 2006, was greater than 450 cells/mm³.

Case Study #1

- She returns to the Oral Health Center for her routine dental hygiene visit. Again, she reports no changes in her general health and well-being.
- An oral exam revealed the following:

Case Study #1

- A new CD4 count was taken in 04/15/07.
- A thorough review of her lab values revealed that her CD4 count is now 43 cells/mm³.
- Working with her primary care provider and nurse educator we were able to convince her to restart therapy.
Candidiasis

- There are three common presentations of candidiasis seen among people living with HIV/AIDS
  - Angular cheilitis
  - Erythematous candidiasis
  - Pseudomembranous candidiasis

Angular cheilitis

Clinical presentation
- Signs: labial commissure
- Fissured, scaley patches
- Unilateral or bilateral
- Symptoms: pain, bleeding
- Burning sensation

Etiology
- Candida albicans

Contributing factors:
- Nutritional deficiency
- Loss of vertical dimension

Diagnosis
- Clinical appearance

Treatment
- Topical anti-fungal
- Resolve contributing factors
Red Lesions
Erythematous candidiasis

Clinical presentation
Signs:
- macular, papillary atrophy
- dorsal tongue, hard palate
- edentulous ridge under denture or removable partial denture

Symptoms:
- asymptomatic or burning sensation

Etiology
- Candida albicans (most common)
- C. glabrata

Diagnosis
- clinical appearance
- cytological smear

Treatment
- topical anti-fungal
Candidiasis

- Three presentations of candidiasis are seen in association with HIV disease:
  - Angular cheilitis
  - Erythematous candidiasis
  - **Pseudomembranous candidiasis**
  - Mild to moderate disease presentation
Question #1
Treatment of candidiasis

- A. Treatment should continue until the symptoms of candidiasis are gone (3 to 7 days)
- B. Treatment of candidiasis should be for 10 days
- C. Treatment of candidiasis should last for 2 weeks.
- D. The answer depends on whether topical or systemic antifungal therapies are used.

Treatment of mild to moderate erythematous and pseudomembranous candidiasis

- Topical agents for mild to moderate oral candidiasis
  - Clotrimazole troches 10 mg: Dispense 70, dissolve one troche in mouth 5 times a day for 14 days
  - Nystatin oral suspension 500,000 units: Swish 5 mL in mouth as long as possible then swallow (optional), 4 times a day for 14 days

Candidiasis

- Three presentations of candidiasis are seen in association with HIV disease:
  - Angular cheilitis
  - Erythematous candidiasis
  - Pseudomembranous candidiasis
    - Mild to moderate disease presentation
    - Moderate to severe disease presentation
Available systemic medications used in the management of moderate to severe oral/esophageal candidiasis

- **Systemic agents**
  - **Fluconazole** 100mg: dispense 15 tablets, take 2 tablets on day 1 followed by 1 tablet a day for the remainder of the 14 day treatment period
  - **Voriconazole** 200mg: dispense 14 tabs, take 1 tab BID for two weeks or at least 7 days following resolution of symptoms.
  - Drug interactions – Contraindications: Rifampin, Rifabutin, Ritonavir and Efavirenz (all potent CYP450 inducers)
Oral hairy leukoplakia

**Clinical presentation**
- White lesions of tongue
- Usually bilateral
- Hairy or shaggy appearance
- Cannot be wiped off

**Symptoms**
- Painless

**Etiology**
- Epstein-Barr virus

**Diagnosis**
- Clinical appearance

**Treatment**
- Usually none required
- High-dose anti-virals
Periodontal Diseases

Linear gingival erythema

Clinical presentation
Signs: - distinctive red band
- free gingival margin
- minimal edema
Symptoms: - minimal bleeding
- mild pain/tenderness

Etiology
unknown

Diagnosis
clinical appearance

Treatment
thorough dental cleaning
chlorhexidine rinse

45

Periodontal diseases

Necrotizing gingivitis

Clinical presentation
Signs: - usually localized
- marginal necrosis
- papillary necrosis
Symptoms: - spontaneous bleeding
- very painful

Etiology
bacteria (gram-negative)

Diagnosis
clinical appearance

Treatment
debridement
antimicrobial rinse
antibiotics

46

Periodontal diseases

Necrotizing “ulcerative” periodontitis

Clinical presentation
Signs: - localized or generalized
- soft tissue necrosis
- alveolar bone necrosis
Symptoms: - tooth mobility
- spontaneous bleeding
- fetid odor
- very painful (“deep-seated” jaw pain)

Etiology
bacteria (gram-negative)

Diagnosis
clinical appearance

Treatment
debridement
antimicrobial rinse
antibiotics

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Severe pain; 1 month duration; strong halitosis

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Oral Warts due to HPV

- Published reports show a markedly increased incidence of oral warts in the cART era * **
Oral sampling for HPV detection and genotyping in HIV-infected patients

- A pilot study to evaluate sampling methods to determine the prevalence of OHPV in HIV+ patients attending the OHC
- Data on demographics, antiviral drug use, sexual history, smoking and alcohol consumption were collected and an oral exam was performed on each participant. An oral rinse with saline solution (OR) and mucosal brushings (BM) were collected. Brushings of tonsils (BT) and oral lesions (BOL) were collected if present. HPV detection and typing were performed on DNA extracts using the Roche Linear Array HPV Genotyping Assay.

Oral sampling for HPV detection and genotyping in HIV-infected patients

- Of the 100 enrolled patients
  - 65% male
  - Median age: 47 years
  - Duration of HIV infection: 14 years
  - Current CD4+: 400 cells/µL
  - 92% on HAART, 84% w/ an undetectable viral load
- HPV was detected in 39% of the oral rinse samples; 24 had high-risk HPV (61.5%) and 17 (43.5%) had multiple types.
- 27 different genotypes isolated
Oral sampling for HPV detection and genotyping in HIV-infected patients

- HPV was detected in 57% of BOL, 13% of BM, and 12% of BT.
- Predictors of multiple types OHPV infection included receptive oral sex, multiple sex partners and a history of anal warts.
- HR-HPV infection was associated with receptive oral sex (OR=3.21, p< 0.05) and a history of oral warts (OR=6.88, p< 0.05).
- CD4+ count, viral load, smoking status, and number of sex partners were not predictive of HR-HPV infections.

HPV and Cancer

- High-risk HPV infection accounts for approximately 5 percent of all cancers worldwide.
- Most high-risk HPV infections occur without any symptoms, go away within 1 to 2 years, and do not cause cancer. These transient infections may cause cytologic abnormalities that go away on their own.

HPV and Cancer

- HPV infections have been found to cause cancer of the posterior oropharynx, (soft palate, the base of the tongue, and the tonsils).
- In the United States, more than half of the cancers diagnosed in the oropharynx are linked to HPV-16
Oral human papillomavirus infection in HIV-negative and HIV-infected MSM.

- In 2010-2011, 794 MSM were included, of whom 767 participants had sufficient data for analysis.
- Median age was 40.1 years [interquartile range (IQR) 34.8-47.5] and 314 men were HIV-infected (40.9%).
- Oncogenic HPV types were detected in 24.8 and 8.8% of oral samples from HIV-infected and HIV-negative MSM, respectively (P<0.001). Of these high-risk types, HPV-16 was the most common (overall 3.4%).
- Oral infection with high-risk HPV was associated with HIV infection in multivariable analysis (P<0.001).


Squamous cell carcinoma

Clinical presentation
Signs: most common locations posterior lateral tongue floor of mouth ventral tongue soft palate highly variable appearance ulceration with raised, rolled margins red, velvety lesion with induration exophytic ulcerated mass mixed red/white lesion white plaque

Symptoms: sometimes painful

Etiology/risk factors
etiology unknown tobacco alcohol nutritional deficiencies human papillomavirus

Diagnosis
incisional biopsy

Treatment
surgical excision radiation therapy Chemotherapy

Pre- & Post- treatment
smoking cessation alcohol cessation aggressive oral health care close follow-up & periodic re-evaluation

Oral Ulcerative Diseases

- HSV
- Aphthous ulcers
- Neutropenic ulcers
- Idiopathic ulcers (ulcers not otherwise specified – NOS)
Herpes Labialis - OHARA Training Slide

Mild to moderate pain for 7 days – similar episodes several times per year - OHARA Training Slide

Recurrent intraoral herpes

Aphthous Ulcer
History of recurrence of similar lesions

Minor Aphthous Ulcers

Major Aphthous Ulcer

Ulcer present 6 weeks – no previous history – Ulcer not otherwise specified (NOS) - OHARA Training Slide
Syphilis

- Syphilis is a systemic disease caused by *Treponema pallidum*. On the basis of clinical findings, the disease has been divided into a series of overlapping stages, which are used to help guide treatment and follow-up.
- *Persons who have syphilis might seek treatment for signs or symptoms of primary infection (i.e., ulcer or chancre at the infection site), secondary infection (i.e., manifestations that include, but are not limited to, skin rash, mucocutaneous lesions, and lymphadenopathy), neurologic infection (i.e., cranial nerve dysfunction, meningitis, stroke, acute or chronic altered mental status, loss of vibration sense, and auditory or ophthalmic abnormalities, which might occur through the natural history of untreated infection), or tertiary infection (i.e., cardiac or gummatous lesions).*

Case study #2

- 49 year old Caucasian male presents with a shallow ulcer approximately 1 cm in diameter on the maxillary anterior buccal mucosa – present 4 weeks – gray/yellow pseudomembrane - painful. Has been using Listerine and believes the ulcer is infected.
- Patient does have a hx. of recurrent aphthous ulcers, but has not had an episode similar to this in 10 years.
- Patient also has a history of lymphoma

Initial diagnosis: *recurrent aphthous ulcer*

Rx. dexamethasone elixir, metronidazole.

CD4: 558 cells/mm³; VL undetectable; all other labs including ANC are normal.

ART: Viramune, Norvir, Invirase, DDI.

Visit 2: pain 3 on 0-10 pain scale. Swelling present. Raised borders – 8mm X 8mm

Rx systemic prednisone – 60 mg X 3 days; 40 mg X 7 days; 20 mg X 7 days
Idiopathic Oral Ulcer

Visit 3; pain 4 on 0 – 10 scale – “does not feel smaller, but it seems smoother”. Patient states that the “pseudomembrane” peels off in the morning.

Clinical exam reveals borders are no longer raised, ulcer is shallow. Dx: idiopathic ulcer somewhat responding to treatment.

Case study #2

Visit 6: Symptoms return, prednisone restarted at 60 mg for 1 week. Crusting noticed on the margin closest to the lip. Acyclovir added as a precaution. Specimen taken to rule out MRSA. Patient noticed “rash/bumps” on scalp. Consider using thalidomide.

Sexual history taken in dental setting.

After consultation with primary care provider, a RPR is ordered primarily due to bumps on scalp and lack of a known reason for oral ulcer.

Results of culture: MSSA+, resistant to Bactrim and Penicillin.

Visit 7: RPR reactive 64 dilution; treatment initiated for syphilis.
Case study #2

- Visit 4: improvement continues, continued prednisone 20mg for an additional week.
- Visit 5: no pain reported, however clinical appearance is worse. Punch biopsy taken.
  - Results: acute and chronic inflammation with vaguely formed histiocytic microgranulomas.
  - Poorly organized epithelial histiocytes – unproven specificity and may be seen in chronic inflammatory diseases such as ulcerative colitis.
  - No evidence of lymphoma, no evidence of carcinoma. AFB negative, no fungal organisms.

Oral Ulcer due to Syphilis – 1 week into therapy

Oral Ulcer due to Syphilis – 3 weeks into therapy

Case #3

- 11/11/11 – received call from a primary care provider to consult on the following case:
  - 49 year old Caucasian male – CD4 count 92 cells/mm³; HIV VL undetectable; WBC 2.7, Platelets 184,000
  - Present medications: tenofovir 300mg, DDI EC 250mg, atazanavir 300mg, norvir 100mg
  - Chief complaint – mouth pain – 10 on a 0 – 10 pain scale
Consult case

Case # 3

- Treated with acyclovir 400mg TID, prednisone 60mg taper, Gelclair (glycyrrhetinic acid/povidone, hyaluronate), percocet, ketoconazole cream 2%
- HSV culture taken; Bacterial culture taken
  - HSV – negative
  - Bacterial culture reveals Staph aureus
Case # 3

- Histoplasma antigen, CBC, platelets, differential and RPR ordered on 12/12/11.
- RPR + - some signs of cognitive decline
- Dx: Neurosyphilis
  - Successfully treated with IV PCN in hospital for 4 days, released on IM procaine PCN plus probenecid

Questions?