ORAL HEALTH AND DISEASE IN HIV

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WE HAVE COME A LONG WAY

- June 5, 1981: 5 cases of PCP in gay men from UCLA (MMWR)

  Pneumocystis Pneumonia = Los Angeles

  In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed Pneumocystis carinii pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.

- July 3, 1981: 26 additional cases

- Dec 10, 1981: 3 NEJM papers describe cases

Gottlieb MS NEJM 2001;344:1788-91
HIV Replication Cycle and Sites of Drug Activity

- Attachment
- Uncoating
- Reverse Transcriptase
- Integrase
- Protease
- Assembly and Release
- NRTIs
- NNRTIs
- Integrase Inhibitors
- Protease Inhibitors

Viral RNA → Unintegrated double stranded Viral DNA → Integrated viral DNA → Viral mRNA → gag-pol polyprotein

Nucleus → Cellular DNA

Capsid proteins and viral RNA

TRUVADA – FDA APPROVED TO PREVENT TRANSMISSION OF HIV
TREATMENT AS PREVENTION

UNDETECTABLE = UNTRANSMITTABLE
NEW HIV CASES IN AMERICA
BUT WE HAVE A WAY TO GO

• Remained stable among gay and bisexual men (MSM), who continue to account for the largest portion (about 70%) of new infections. Trends varied by race/ethnicity and age:
  • By race/ethnicity, new cases remained **stable** among black MSM; **increased 30%** among Latino MSM; and **decreased 16%** among white MSM
  • By race/ethnicity and age, new cases **decreased more than 30%** among **black MSM ages 13 to 24**; remained stable among Latino MSM ages 13 to 24; and **increased about 65%** among both **black and Latino MSM ages 25 to 34**.
NEW HIV CASES IN AMERICA

• Decreased about 17% among heterosexual men and women including a 15% decrease among heterosexual African American women
• Decreased 30% among people who inject drugs, but appear to have stabilized in more recent years. (opioid epidemic – Scott County, Indiana ~ 200 cases)

• CDC estimates that the decline in HIV infections has plateaued because effective HIV prevention and treatment are not adequately reaching those who could most benefit from them.
• These gaps remain particularly troublesome in rural areas and in the South and among disproportionately affected populations like African-Americans and Latinos.
PEOPLE WITH UNTREATED HIV TRANSMITTED 80% OF NEW INFECTIONS

• 15% who did not know their status accounted for 38% of new cases
• 23% who knew their status but were not in care accounted for 43% of new cases
• 11% in care but not virally suppressed accounted for 20% of new cases
• 51% virally suppressed accounted for 0 New cases
PLAN TO END HIV

HIV Infections Started to Stabilize in 2013

For more information, visit cdc.gov/nchhstp/newsroom
PLAN TO END HIV

GOAL:
75% reduction in new HIV infections in 5 years and at least 90% reduction in 10 years.

www.hiv.gov
PLAN TO END HIV

Diagnose all people with HIV as early as possible after infection.

Treat the infection rapidly and effectively to achieve sustained viral suppression.

Protect people at risk for HIV using potent and proven prevention interventions, including PrEP, a medication that can prevent HIV infections.

Respond rapidly to detect and respond to growing HIV clusters and prevent new HIV infections.

HIV HealthForce will establish local teams committed to the success of the Initiative in each jurisdiction.
50 COUNTIES AND 7 STATES TARGETED TO START
HIV ORAL DISEASES APP

HIV Oral Diseases
Diversified Animated Technologies Associates, Inc.

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Use of high-speed ultrasonic scalers

Which of the following statements is true?

- #1 It is safe to use a high-speed ultrasonic scaler on a person with an AIDS diagnosis.
- #2 It is NOT safe to use a high-speed ultrasonic scaler on a person with an AIDS diagnosis.
Q. What is the risk of transmission of bloodborne pathogens (e.g., HIV) through aerosols generated during the use of an ultrasonic scaler or high speed dental drill?

- Aerosols are invisible particles, less than 10 microns in diameter, generated by both human and environmental sources that have the capability to remain airborne for extended periods in the indoor environment.
- There is no clear evidence that powered dental and surgical instruments can generate aerosols containing infective bloodborne pathogens.
A 28-year-old HIV-infected male is in need of comprehensive dental care including two dental extractions, periodontal scaling and root planing and multiple dental restorations.

The patient initially presents with an acute dental emergency.
CASE STUDY

• The patient’s medical history:
  • *Pneumocystis pneumonia* three months ago, which is when he was diagnosed with Stage 3 HIV (AIDS) in the hospital
  • Patient presents with a *moderate case of oral pseudomembranous candidiasis* at the time of his emergency dental visit.

• Present medications:
  • *Bactrim DS* (sulfamethoxazole and trimethoprim) used to prevent *Pneumocystis pneumonia*.
  • *Azithromycin 1 gm* once per week (used to prevent DMAC)
  • Not presently on cART
  • NKDA
CASE STUDY – LAB VALUES

- **CD4 count**: 50 cells/mm$^3$
- **VL**: $> 150,000$ copies/mL
- **Hg**: 10.0 g/dl
- **Platelet count**: 75,000/mm$^3$
- **Absolute Neutrophil Count (ANC)**: 1,000 cells/mm$^3$
You are interested in obtaining medical “clearance”. Which of the following statements are true?

A. Any HIV infected patient with a CD4 count less than 200 cells/mm³ (stage 3 HIV) should be pre-medicated prior invasive dental procedures.

B. Candidiasis should be treated prior to initiating dental therapy to prevent a fungal septicemia.

C. CD4 count and HIV viral load do not have an impact on the provision of routine/emergent dental care.
DENTAL TREATMENT CONSIDERATIONS

• Evidence-based research has proven that providing dental care for the vast majority of people living with HIV/AIDS is no different than providing care for the general patient population.
  • Evidence Report/Technology Assessment No. 37, Management of Dental Patients Who Are HIV Positive (AHRQ Publication No. 01-E042)
DENTAL COMPLICATIONS AFTER TREATING PATIENTS WITH AIDS.
GLICK M., ABEL S., ET AL JADA 125:1994

• **331 patients** (average CD4 count of 71 cells/mm³) **1,800 invasive dental procedures** (defined as the breaking of the mucosal membrane) were performed.

• **RESULTS:** The number of post-procedural complications was only 17, representing an overall **complication rate of 0.9%**

• **CONCLUSIONS:** Incidence of post-procedural complications is no greater than in other populations
IMPORTANT LAB VALUES

• **CD4 count**¹
  - No need to pre-medicate prior to invasive dental care no matter how low.

• **HIV Viral Load**¹
  - No need to pre-medicate prior to invasive dental care no matter how low.

• **Platelet count**¹
  - Normal – male/female: 150,000 – 450,000 per microliter (mcl) of blood
  - **Dental procedures can safely be performed with a platelet count of 60,000 mcl or greater**

IMPORTANT LAB VALUES

• INR for patients on warfarin
  • No alteration of anticoagulation is necessary for INR that is in therapeutic range (INR 1-3), given that local hemostatic measures are used.²

• Absolute Neutrophil Count¹
  • **An Absolute Neutrophil Count <500 cells/mcl requires premeditation prior to invasive dental procedures.**
    • Follow the American Health Association/ADA guidelines

• Glucose/ A1c
  • A1c > 8% is poorly controlled; <7% is well controlled.

• ²J Am Dent Assoc, Vol 134, No 11, 1492-1497. © 2003 American Dental Association
QUESTIONS

• How many dental healthcare professionals have seroconverted after an exposure in the dental setting?

• Since the year 2000, how many healthcare workers have seroconverted after an exposure?
# Risk of Infection After Needlestick

<table>
<thead>
<tr>
<th>Source</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
<td>6.0-30.0%</td>
</tr>
<tr>
<td>HCV</td>
<td>1.8%</td>
</tr>
<tr>
<td>HIV</td>
<td>0.3%</td>
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</tbody>
</table>
TIMING + DURATION OF PEP

• PEP is most effective when begun soon after the exposure, less effective as time increases (animal studies)
  • PEP should be started as soon as possible after the exposure, preferably within TWO hours.
  • Point at which no benefit may be gained is not defined; in animal studies less effective if started >72 hours after exposure

• Optimal duration unknown; **4 weeks** appeared protective in occupational and animal studies
  • PEP should be taken for 4 weeks, if tolerated
HIV oPEP: What to Give

Three-drug oPEP regimens are now the recommended regimens for all exposures.

Guidelines no longer require assessing the degree of risk for the purpose of choosing a “basic” two-drug regimen vs. an “expanded” three-drug regimen.

There are some special circumstances, however, in which a two-drug regimen can be considered/used, especially when recommended antiretroviral medications are unavailable or there is concern about potential toxicity or adherence difficulties. In addition,

https://nccc.ucsf.edu/clinical-resources/pep-resources/pep-quick-guide/
**Preferred HIV 3-Drug Occupational PEP Regimen:**

Truvada™ 1 tablet by mouth once daily  
[co-formulated Tenofovir DF (Viread®; TDF) 300mg + emtricitabine (Emtriva™; FTC) 200mg] for 28 days

**PLUS**

dolutegravir (Tivicay™) 50mg PO once daily  
Duration: 28 days

or

raltegravir (Isentress®; RAL) 400mg by mouth twice daily for 28 days

https://ncc.ucsf.edu/clinical-resources/pep-resources/pep-quick-guide/
• Preferred HIV PEP regimen:
  • If you take a dolutegravir-containing regimen at the time of becoming pregnant and during the first trimester of pregnancy, there is a risk that your baby may develop **neural tube defects**. Neural tube defects happen early in pregnancy, before many women even know they are pregnant.

• For this reason, women of childbearing age should talk to their health care professional about other non-dolutegravir-containing antiretroviral medicines (e.g. Raltegravir)
SOURCE PATIENT HIV TESTING

• If possible, determine the HIV status of exposure source patient to guide appropriate use of PEP
  • For sources whose HIV status is unknown, rapid HIV testing facilitates decisions about need to initiate or continue PEP
  • Investigation of whether a source patient might be in the window period before HIV seroconversion is not necessary, unless acute retroviral syndrome is suspected
  • 4th-generation HIV Ag/Ab tests allow identification of most HIV infections during the window period
Follow-up testing
- HIV testing at baseline, 6 weeks, 12 weeks, and 4 months after exposure
- HIV testing for any exposed HCP with symptoms compatible with acute retroviral syndrome, regardless of interval since exposure
- If HIV infection is identified, refer for HIV care
- Report case to state health department and to CDC COPHI coordinator (404-639-2050)
Clinician-to-clinician assistance with PEP-related decisions

AETC National Clinician Consultation Center's (NCCC) Post-Exposure Prophylaxis Hotline (PEPline): 888-HIV-4911 (888-448-4911) 9:00 AM - 9:00 PM ET, 7 days/week

The AETC NCCC PEPline works with providers to:

- Assess the risk of exposure
- Determine the appropriateness of prescribing PEP
- Select the best PEP regimen
- Provide recommendations for follow-up testing
ORAL MANIFESTATION SEEN IN ASSOCIATION WITH HIV INFECTION

- 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-combination antiretroviral therapy (cART) to 32-46% post cART.
- (Patton et al. 2000; Schmidt-Westhusen et al. 2000; Gaitan Cepeda et al. 2008; Tami-Maury IM et al. 2011)
- Factors, which predispose expression of oral lesions, include:
  - CD4 counts less than 200 cells/mm3
  - Viral load greater than 3,000 copies/mL
  - xerostomia (dry mouth)
  - poor oral hygiene
  - smoking
  - Present smoking is the major modifiable death risk for people living with HIV/AIDS (PLWHA)
- Including smoking cessation education and referral is a very important component of overall care for PLWHA.
- There are not any oral lesions that are diagnostic of HIV infection, however they can be suggestive of underlying disease process including HIV, diabetes, etc.
- Present research reveals that oral candidiasis is still the most prevalent oral lesions seen in association with HIV disease.
Angular Cheilitis

OVERVIEW

Angular cheilitis may have a number of etiologies (nutritional deficiency, decreased vertical dimension of occlusion, or local habits coupled with an inflammatory response). In PLWH it is important to assume that these lesions have fungal infiltrates. Angular cheilitis develops at the commissures of lips (corners of the mouth), and the area can crack easily.

DIAGNOSIS

Diagnosis is determined by the clinical presentation. Special tests or staining is not required.

TREATMENT

Avoid treatment combinations that include steroidal components, which may further suppress the immune system. For instance, Mycolog-Il cream and Lotriderm contain corticosteroids. Ketoconazole (2%) cream, clotrimazole (1%) cream, and nystatin (100,000 units/gram) cream are effective in controlling angular cheilitis. All of these agents should be applied directly to the affected areas 4 times per day for 14 days.
CANDIDIASIS

• Three presentations of candidiasis are seen in association with HIV disease:
  • Angular cheilitis
  • Erythematous candidiasis
  • Pseudomembranous candidiasis
ERYTHEMATOUS CANDIDIASIS
ERYTHEMATOUS CANDIDIASIS
MILD TO MODERATE
PSEUDOMEMBRANOUS CANDIDIASIS
MODERATE TO SEVERE PSEUDOMEMBRANOUS CANDIDIASIS
## OVERVIEW

Pseudomembranous candidiasis is the most common intraoral opportunistic infection seen in association with HIV infection. Pseudomembranous candidiasis typically presents as a white, cottage cheese-like, patchy lesion. It can be wiped off, leaving erythematous (red) and potentially bleeding tissue underneath. It can appear anywhere within the oropharynx. Thrush, or pseudomembranous candidiasis, is usually caused by Candida albicans, but there has been an increased incidence of candidiasis due to non-albicans species, which can be more difficult to treat.

## DIAGNOSIS

Diagnosis of pseudomembranous candidiasis is most frequently based on the clinical appearance. In many instances it is very easy to diagnose by seeing if a portion of the lesion will wipe away. Simply take the wooden tip of a cotton tip applicator and gently try to brush away a portion of the affected area.

A KOH (potassium hydroxide) preparation can be used to find out whether a fungal infection is present. A sample is taken by lightly scraping the affected area. The sample is placed on a slide with KOH solution. This solution slowly dissolves the oral mucosal cells.

## Treatment

Treatment of pseudomembranous candidiasis is based on the extent of the infection. For mild to moderate cases (slides 2 and 3) topical antifungal medications are the treatment of choice.

<table>
<thead>
<tr>
<th>Oral troches (lozenges)</th>
<th>Rx: clotrimazole 10 mg Disp. 70 troches Sig. Dissolve 1 troche in mouth 5x/day X 14 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antifungal rinses</td>
<td>Rx: nystatin oral suspension 5000,000 U Disp. 280 ml Sig. Swish 5 ml (1 teaspoon) in mouth 2 minutes, QID X 14 days</td>
</tr>
</tbody>
</table>

Of note, nystatin oral suspension should not be swallowed. Also, this suspension has a very high sugar content that could exacerbate untreated dental decay.

<table>
<thead>
<tr>
<th>Systemic therapy</th>
<th>Rx: fluconazole 100 mg Disp. 15 Sig. Take 2 tabs for the initial dose, then 1 tab/day X 14 days</th>
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<tbody>
<tr>
<td></td>
<td>For esophageal candidiasis (slide #8) a higher dose of fluconazole is indicated.</td>
</tr>
<tr>
<td></td>
<td>Systemic therapy</td>
</tr>
<tr>
<td></td>
<td>Rx: fluconazole 200 mg Disp. 22 Sig. Take 2 tabs for the initial dose, then 1 tab/day X 21 days</td>
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For patients who have acrylic partial or complete dentures, it is very important to treat the appliance as well. This can be done by either soaking the appliance in a 1:1 mixture of water and 0.12% chlorhexidine gluconate (e.g. PerioGard) solution overnight. Other options include placing any of the topical creams to the inside of the appliance or soaking the removable prosthesis in a weak solution of bleach and water for a few minutes daily.
ORAL HAIRY LEUKOPLAKIA

OHARA TRAINING SLIDE
TWENTY-FIRST-CENTURY ORAL HAIRY LEUKOPLAKIA-A NON-HIV-ASSOCIATED ENTITY.

• Objective
  • This study presents the clinicopathologic features of a series (N = 35) of patients with non-human immunodeficiency virus (HIV)-associated oral hairy leukoplakia (OHL).

• Results
  • 28 patients had intercurrent respiratory problems requiring long-term steroid inhaler use, four suffered from autoimmune diseases requiring immunosuppressant therapy, and four had diabetes. The majority of lesions were located on the tongue, and 24 showed evidence of Candida co-infection
• Kaposi’s Sarcoma

RETURNS

• 3 cases diagnosed in one week at the IDP (10/19/16 – 10/23/16)
• All 24 years or younger
• 2 of 3 were non-compliant with cART
• Causative agent: HHV8
KAPOSI’ SARCOMA

- Treatment involves cART and chemotherapy.

OVERVIEW

Kaposi’s sarcoma (KS) is a vascular neoplasm associated with the human herpes virus 8 (HHV8) that has been of special concern since early in the HIV epidemic. KS is most common oral malignancy seen in association with HIV disease.

DIAGNOSIS

Diagnosis is based on biopsy.
PERIODONTAL DISEASES

• Necrotizing Ulcerative Gingivitis

• Necrotizing Ulcerative Periodontitis
SEVERE PERIODONTITIS IS MORE COMMON IN HIV-INFECTED PATIENTS

- The study assessed prevalence and severity of periodontitis in 258 HIV-infected patients and 539 historical controls with the Dutch Periodontal Screening Index (DPSI).

- Severe periodontitis (DPSI 4) was more prevalent in HIV-infected patients than in controls (66% vs. 36%, p = 0.002).

- HIV-infection, increasing age and male gender were significant risk factors for severe periodontitis.

- CONCLUSIONS: Awareness of the increased prevalence of periodontitis associated with HIV-infection among patients and health-care professionals could significantly improve oral health and quality of life of HIV-infected patients.
SEVERE PAIN; 1 MONTH DURATION;
STRONG HALITOSIS
RECURRENT INTRAORAL HERPES

OHARA TRAINING SLIDE
MILD TO MODERATE PAIN FOR 7 DAYS – SIMILAR EPISODES SEVERAL TIMES PER YEAR
HISTORY OF RECURRENTNESS OF SIMILAR LESIONS
ULCER PRESENT 6 WEEKS – NO PREVIOUS HISTORY – ULCER NOT OTHERWISE SPECIFIED (NOS) - OHARA TRAINING SLIDE
Human Papilloma Virus (HPV) is the cause of oral warts/condylomas. Lesions can be flat, raised, hyperkeratinized, or cauliflower-like in appearance. They can be singular or multiple. Oral warts are not associated with oncogenic types (cancer). However, one pilot study did find that patients who presented with oral warts were significantly more likely to have high risk types present. These results were thought to be due to the mode of transmission.
HPV AND HIV – ORAL CAVITY PERSISTENCE.

• Human papillomavirus infection in the oral cavity of HIV patients is not reduced by initiating antiretroviral therapy.
  • Among 388 participants, 18% had at least one HPV genotype present before initiating ART, and 24% had at least one genotype present after 12-24 weeks of ART.
  • Shiboski CH et al. AIDS. 2016 Feb 25
HPV AND HIV – ORAL CAVITY PERSISTENCE.

• These results suggest:
  1) **effective immune control of HPV in the oral cavity of HIV-infected patients is not reconstituted by 24 weeks of ART**;
  2) while ART initiation was not followed by an increase in oral warts*, we observed an increase in oral HPV DNA detection after 12-24 weeks.
  3) **The prevalence of HPV-associated oral malignancies may continue to increase in the modern ART era.**
    • Shiboski CH et al. Human papillomavirus infection in the oral cavity of HIV patients is not reduced by initiating antiretroviral therapy. AIDS. 2016 Feb 25
NHANES: RISK FOR HPV-RELATED ORAL CANCER SOARS IN US MEN

• High-risk oral HPV infections were higher among men compared with women (7.3% [7 million] vs 1.4% [1.4 million]; P<.001).

• **Prevalence of HPV 16**, which increases risk for oropharyngeal squamous cell carcinoma (OPSCC), is **6-fold greater in men than in women**.
  • Annals of Int Med, Oct 2017
NHANES: RISK FOR HPV-RELATED ORAL CANCER SOARS IN US MEN

• Oral HPV infection prevalence was 29.8% among men with ≥16 lifetime oral sexual partners, 18.2% among men who reported having sex with men, and 19.3% among men with concurrent genital HPV infection.

• Overall oral HPV prevalence was 11.5% in men and 3.2% in women.
  • Annals of Int Med, Oct 2017
ORAL CANCER 3X MORE LIKELY TO OCCUR IN MEN AS IN WOMEN.

In the period 2011-2015, oral cancer occurred nearly three times as often in males as in females.

In the period 2011-2015, tongue and throat cancers (malignant neoplasms of the tongue and of the nasopharynx, hypopharynx and oropharynx) were much more likely to occur in males than females.
SQUAMOUS CELL CARCINOMA

OVERVIEW

PLWH have an increased incidence of many types of malignancies, including those associated with the oral cavity. The most common type of oral cancer in the general population is squamous cell carcinoma (SCC), which accounts for 90% of all oral cancers. Squamous cell carcinoma typically presents in the posterior oropharynx and base/lateral border of the tongue.

The landscape of oral malignancy is changing in the general population as well as in PLWH. Risk factors for squamous cell carcinoma have traditionally been
QUESTIONS?
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