HIV: oral manifestations, monitoring and dental management

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THANK YOU!

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No disclosures except the support that these giants of oral medicine so unselfishly gave to me.
On June 5, 1981, when the Centers for Disease Control (CDC) reported five cases of *Pneumocystis carinii* (now *jiroveci*) pneumonia in young homosexual men in Los Angeles, few suspected that it heralded a pandemic of acquired immunodeficiency syndrome (AIDS).

In 1983, a retrovirus :HTLV-III (later named the human immunodeficiency virus [HIV]) was isolated from a patient with AIDS.
“Today’s discovery represents the triumph of modern science over a dreadful disease.”

HEW Secretary
Margaret Heckler 1983
upon the discovery of HTLV-III
HIV

- 2016: 70 million, worldwide
- 29 million deaths from AIDS !!
- infected women (world) ~40%
- >1.5 million infected children (90% = 3rd world)
- >65% in Africa
- >60% of all hospital beds
- Decreased life expectancy >15 years!
HIV-US. 2016

- U.S. > 13.8:100,000
- AIDS: U.S. > 1.2 million cases
- AIDS: U.S. > 570,000 deaths
- changes in epidemiology
  - homosexual-bisexual males
  - IVDUs
  - women
  - children
HIV-AIDS in the U.S.

- cases of AIDS-1996 = ~ 56,000
- deaths from AIDS-1996 = ~ 45,000
- cases of AIDS-2008 = ~ 25,000
- deaths from AIDS-2008 = ~ 10,000
- cases of AIDS-2016 = ~ 15,000
- deaths from AIDS-2016 = ~ 7,000
source: CDC- 2016

- AIDS new cases
- Deaths
- alive with AIDS

Cases per wk:
- 1990
- 1992
- 1998
- 2012
Incubation Period to AIDS

Transfusion Recipients: 7 years
Hemophiliacs: 10 years
Injecting drug users: 10 years
Homosexual/bisexual men: 8-12 years

Cumulative %
0% 3% 12% 36% 53% 68% 85%
1yr 3yr 5yr 8yr 10yr 14yr 20yr
Most untreated patients have HIV-1 RNA levels stabilize between 1000-10,000 copies/mL. In AIDS, levels > 1 million copies/mL.
The definition of AIDS provided by the CDC has been revised several times over the years, and in 2008 it was revised to be laboratory-confirmed evidence of HIV infection in a person who has stage 3 HIV infection (i.e., a CD4+ lymphocyte count less than 200 cells/µL). This definition also includes HIV-infected persons whose CD4+ count may be above 200 but have an AIDS-defining condition.
AIDS defining diseases*

- Pneumocytis pneumonia 38%
- HIV wasting syndrome** 18%
- Candidal esophagitis 14%
- Kaposi’s sarcoma 10%
- TB 10%
- Lymphoma 10%
  Viral: Herpesviridae, CMV, HPV, Pox family
- Neurologic < AIDS-related pain (neuropathy, myelopathy)

** loss of 10% body wt. < 30days
Clinical category C

Bacterial infections, multiple or recurrent*
Candidiasis, respiratory
Candidiasis, esophageal
Coccidioidomycosis
Cryptosporidiosis
disease=
Cytomegalovirus retinitis
Cytomegalovirus
Encephalopathy, HIV
related
Herpes simplex= chronic; respiratory; esophageal
Histoplasmosis=
HIV wasting syndrome
HIV-related=
Isosporiasis
Lymphoid interstitial pneumonia*
Lymphoma, immunoblastic=
Lymphoma, primary; brain
M. avium complex=
M. tuberculosis=, disseminated; extrapulmonary

Cervical cancer**
Cryptococciosis= Cryptosporidiosis Cytomegalovirus

Encephalopathy, HIV

HIV encephalopathy
Immunosuppression, severe

Kaposi’s sarcoma=
Lymphoma, Burkitt’s=
Lymphoma, brain

Dental patient management: AIDS

- Opportunistic infections
  - Pneumocystis carinii pneumonia (PCP)
  - Toxoplastic encephalitis
- TB
  - Mycobacterium avium complex (MAC)
  - Streptococcal pneumonia
- CMV
- Candidiasis
- Cancer: lymphoma, SCC, Kaposi’s
Treatment of HIV Infection

- Most untreated patients have HIV-1 RNA levels stabilize between 1000-10,000 copies/mL. In AIDS, levels > 1 million copies/mL.

- Combination therapy of NRTI + NNRTI + HIV Protease inhibitor

- Up to 28% of newly infected individuals may contract HIV that is resistant to one or more anti-AIDS drugs.

HIV Therapy Edge is software to search gene sequences for over 120 drug resistance mutations and to report which drugs to avoid.
Antiretroviral Therapy

- Preferred Antiretroviral Regimens
- Backbone for Rx- naïve patients: dual NRTI Rx
  - Optimal: 2 NRTIs + PI (or II);
  - 2 NRTIs + NNRTI
  - Less desirable: 3 NRTIs
  - Unacceptable: monotherapy

Walmsley S et al. Dolutegravir plus abacavir/lamivudine for the treatment of HIV-1 infection in antiretroviral therapy-naïve patients:
Antiretroviral Therapy

- Resistance

<table>
<thead>
<tr>
<th>Year</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>1%</td>
</tr>
<tr>
<td>1994</td>
<td>7%</td>
</tr>
<tr>
<td>2016</td>
<td>22%</td>
</tr>
</tbody>
</table>

Changing therapy: failure (rising viral load, falling CD4 count, symptoms, ADEs) never add a single drug to a failing regimen, begin with at least 2 drugs. (i.e. Dual Tx- NRTI backbone

Add integrase inhibitor
Add NNRTI
### Anti-HIV Drugs

#### Nucleoside RT Inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Cost 30 day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir (ABC; Ziagen)</td>
<td>300 bid</td>
<td>$349</td>
</tr>
<tr>
<td>Didanosine (ddI, Videx)</td>
<td>200 bid</td>
<td>217</td>
</tr>
<tr>
<td>Lamivudine (3TC, Epivir)</td>
<td>150 bid</td>
<td>259</td>
</tr>
<tr>
<td>Stavudine (d4T, Zerit)</td>
<td>40 bid</td>
<td>274</td>
</tr>
<tr>
<td>Zalcitabine (ddC, Hivid)</td>
<td>0.75 tid</td>
<td>212</td>
</tr>
<tr>
<td>Zidovudine (AZT, ZDV, Retrovir)</td>
<td>200 tid</td>
<td>604</td>
</tr>
<tr>
<td>Zidovudine + Lamivudine (Combivir)</td>
<td>1 tab bid</td>
<td>564</td>
</tr>
</tbody>
</table>

#### Nucleotide RT Inhibitor

- Adefovir 120 qd only available thru EAP

#### Non-nucleoside RT inhibitors (NNRTI)

- Delavirdine (Rescriptor) 400 tid 239
- Efavirenz (EFV, Sustiva) 600 qd 394
- Nevirapine (Viramune) * 200 bid 279

*Not drug of choice for HIV postexposure prophylaxis
Protease Inhibitors: block an enzyme that cleaves Gag and Gag-Pol polyproteins - 50 to 100X more potent than AZT

<table>
<thead>
<tr>
<th>Inhibitor</th>
<th>Dose</th>
<th>Frequency</th>
<th>Cost Per Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amprenavir (Agenerase) 50s, 150s</td>
<td>1200</td>
<td>bid</td>
<td>$605</td>
</tr>
<tr>
<td>Indinavir (Crixivan)</td>
<td>800</td>
<td>q8h</td>
<td>$464</td>
</tr>
<tr>
<td>Nelfinavir (Viracept)</td>
<td>750</td>
<td>tid</td>
<td>$583</td>
</tr>
<tr>
<td>Ritonavir (Norvir)</td>
<td>600</td>
<td>tid</td>
<td>$668</td>
</tr>
<tr>
<td>Saquinavir (Invirase)</td>
<td>600</td>
<td>tid</td>
<td>$586</td>
</tr>
</tbody>
</table>
AIDS treatment

- complex Rx: 1-8 months > $12,000.00
- poor compliance
- HIV +ve & infectious
- viral genotyping to detect antiretroviral resistance
AIDS treatment

- status (CD4 count and viral load)
- HIV +ve & infectious
- viral genotyping to detect antiretroviral resistance

Opportunistic infections!

- CD-4 counts >500; esp. >200
Principles of medical management of dental patients

- Detection
- Physical Evaluation
- Medical treatment
- Status
- Management
H1N1 in 2016:
US = 13,000 deaths
Seasonal flu = >36,000 deaths
"FLU UPDATE"

I give up...

What is the difference between Bird Flu and Swine Flu?

For bird flu you need tweetment and for swine flu you need oinkment
Management Considerations

- Viral load will determine level of viremia, efficacy of antiretroviral therapy, disease progression, and prognosis, thus influencing appropriate treatment planning.
- There is no need for prophylactic medication prior to dental therapy based solely on viral load.
Management Considerations

- Dental treatments, including extractions, can be safely performed in patients with platelet counts >50,000 platelets/mm$^3$.
- Prophylactic bactericidal antibiotics need to be considered when the neutrophil (ANC) count drops below 500 cells/mm$^3$ (normal 2,500-7,000 cells/mm$^3$), but at this stage the patient is often already medicated with antibiotics due to frequent bacterial infections and as prophylaxis against opportunistic infections.
There are very few complications associated with dental care of HIV-infected patients and most infected patients can be safely treated by general dental practitioners.

Oral lesions found in HIV-infected persons are reliable markers for immune suppression, disease progression and AIDS.
The prevalence and incidence of oral manifestations of HIV has been demonstrated to be influenced by a number of mutable and immutable factors: gender, transmission behaviours, immune status, viral status, medication use, comorbidities, environmental factors and other behavioural factors. In general, it is accepted that oral candidiasis is still the most common oral lesion related to HIV.

SJ Challacombe. Oral Dis - April 1, 2016; 22 Suppl 1 (1); 120-7. DOI: 10.1111/odi.12408
GROUP 1 ORAL LESIONS
Strongly Associated with HIV Infection

- Candidiasis
- Oral hairy leukoplakia
- Kaposi’s sarcoma
- Non-Hodgkin’s lymphoma
- Periodontal disease - linear gingival erythema, necrotizing (ulcerative) gingivitis, necrotizing (ulcerative) periodontitis

Oral candidiasis most common oral lesion among HIV+ persons (39.6%), then hairy leukoplakia (26.3%), exfoliative cheilitis (18.3%), and linear gingival erythema (LGE) (11.5%). JOPM 2001 30(4):224-30 in Thailand
The overall prevalence of oral manifestations has changed significantly since the advent of HAART (approximately 10%)\(^{34-38}\)

Several studies have shown reductions in oral lesions in those on antiretroviral therapy (Patton et al, 2000; Schmidt-Westhausen et al, 2000; Greenspan et al, 2001; Ramírez-Amador et al, 2003; Miziara et al, 2006; Umadevi et al, 2007).

In spite of these apparently encouraging results, it can be estimated that oral lesions in HIV infection remain untreated in up to 10 million people. HIV-related oral abnormalities are present in 30–80% of HIV infected individuals before therapy and the abnormalities are often inaccurately described in medical care (Hilton et al, 2001).
Oral lesion in AIDS

- 2016 Meta-analysis of 97 studies:
  - Overall prevalence of oral lesions - 10.2%
  - #1 candidiasis 26.2 %
  - HAART has little impact on most lesions
  - Some slightly less/others more frequent
  - Indicator of overall immunosuppression
Oral candidiasis in HIV

- prevalent (~30%)
- related to other oral diseases (i.e. caries and periodontal disease, HSV, etc.)
- proportional to low CD-4 counts
- predictive of rapid progression to death
HIV Infection

- Angular cheilitis
- Patient was HIV infected
- candidiasis with AIDS
Candidiasis- Rx

- Clotrimazole 60 mg troches qid
- Fluconazole 100 mg qd
- 400 mg suspension of posaconazole
- Echinocandin- IV

Nittayantanta W. Oral Dis - April 1, 2016; 22 Suppl 1 (1); 120-7. DOI: 10.1111/odi.12394
Lymphoma

- SIGNS
- pallor, petechiae, ecchymoses

lymphadenopathy
- gingival bleeding, hypertrophy
- oral lesions, loose teeth, pulpal path
Non-Hodgkin’s LYMPHOMA

- Usually multifocal, non-localized
- 10% have AIDS
- B-cell origin = 90%
- 66% present with non-painful lymphadenopathy
- Extranodal lesions
HIV and SGD

- SGD: SG hypertrophy
- Mean CD4+ <280
- Hyposalivation; WUS < 0.1 ml/min.
- SS-like T-cell infiltrate
- Altered salivary composition (sIgA, albumin, lysozyme, protein)


Increase with ART

- There was an increase in salivary gland disease and a striking increase in warts on ART (Greenspan et al, 2001; Tappuni and Fleming, 2001).
Human Papillomavirus

- Condyloma acuminatum
- Transmission
  - HPV DNA detected in sperm 32% of men detected in 24 of 45 men hx or clinical evidence of HPV infection
Oral Hairy Leukoplakia
However, HL has not completely disappeared in the era of antiretroviral therapy (ART). HL persistence in the presence of ART was confirmed in a recent domestic and international clinical trial, ACTG-A5254, of over 300 HIV-infected individuals (Shiboski et al., 2015). HL comes and goes and was seen to respond to zidovudine in an observational trial (Katz et al., 1991). HL responds to some anti-EBV preparations including acyclovir, desciclovir, and valacyclovir (Resnick et al., 1988; Greenspan et al., 1990; Walling et al., 2003a,b).
Bacterial Infections

- Systemic Infections
- Oral Infections
  - Periodontal tissues
    - Necrotizing ulcerative gingivitis (NUG)
    - Linear gingival erythema
    - Necrotizing ulcerative periodontitis
  - Tongue and other mucosal structures
HIV Infection

- Linear gingival erythemia
Necrotizing Ulcerative Periodontitis
HIV Infection

- Kaposi’s sarcoma
HIV Infection

- Recurrent herpes simplex infection in a patient with AIDS
HIV Infection

- Herpes zoster
- Outbreak occurred in patient with AIDS
HIV Infection

- Aphthous ulceration (major type)
- Patient was diagnosed with AIDS
8 editions since 1982
>160,000 copies sold

- 43 U.S. Dental schools
- 4 Canadian Dental schools
- International
5 languages besides English
DENTAL MANAGEMENT OF THE MEDICALLY COMPROMISED PATIENT

A. antibiotics (prophylaxis, prone to infections, etc.)
   anesthetics (epinephrine)
   allergies, adverse reactions, analgesics

B. bleeding
   breathing
   blood pressure, bacteremias (infections)

C. complications
   Medical- systemic-ROS immunocompromised
   cardiac (arrhythmias, arrest, stress, reserve-output, etc.)
   cardiovascular (other...vital signs, etc.)
   consciousness

D. drugs (side effects, allergies, adverse reactions, interactions, etc.)
   devices, delayed healing

E. emergency treatment (medical, dental)

F. follow up
Dental Management of the Patient With End-Stage Renal Disease

UNDER CONSERVATIVE CARE

P: Patient Evaluation and Risk Assessment (see Box 1-1)
   Evaluate and determine whether renal disease exists.
   Obtain medical consultation if poorly controlled, undiagnosed, or if uncertain.

Potential Issues or Concerns

A: **Analgesics**: Dosage adjustment likely when GFR < 60. Avoid long-term use of NSAIDs in CKD. Avoid narcotics in CKD because these drugs can cause prolonged sedation and respiratory depression.
   **Antibiotics**: Dosage adjustments likely when GFR < 60. Aggressively manage orofacial infections with culture and sensitivity tests and antibiotics. Consider hospitalization for severe infection or major procedures. A loading dose may be required when infection and CKD are concurrent.
   **Anesthetics (local)**: Dosage adjustment generally not required.
   **Anti-anxiety**: No dosage adjustment for single dose benzodiazepines.

B: **Bleeding**: Screen for bleeding disorder before invasive procedures. Pay meticulous attention to good surgical technique. Excessive bleeding may occur in the untreated or poorly controlled patient. Have available topical anticoagulants for use.
   **Blood pressure**: Monitor blood pressure closely as hypertension is common in CKD. Refer patient if pressure is elevated.

C: **Chair position**: If on antihypertensive medication, re-equilibrate patient in upright position before exiting dental chair.

D: **Devices**: No concerns
   **Drugs (interactions, allergies or supplementation)**: Adjust dosage of drugs metabolized by the kidney when GFR is < 60, per Table 13-4. Avoid nephrotoxic drugs (aminoglycosides, acetaminophen in high doses, acyclovir, aspirin, nonsteroidal antiinflammatory drugs).

E: **Emergencies**: Minimize risk for emergencies by avoiding invasive procedures and long appointments if disease is unstable (poorly controlled or advanced [CKD ≥3]).
Dental management

- A. Antibiotics
  - May need antibiotics (as prophylaxis/or coverage) if low CD4 (or WNC) count.
- Analgesia:
  Avoid aspirin and other NSAIDs in pt with thrombocytopenia.
Dental management

B. Bleeding:

- Excessive bleeding may occur in the pt with untreated/poorly controlled disease and/or thrombocytopenia; may have co-morbid conditions (i.e. liver disease, etc.)
- BP - possible HTN with ART
Dental management

- C. Cardiovascular:
  - Confirm cardiovascular status. Some ART drugs can increase risk of HTN and/or arrhythmias and cardiovascular disease (CHF).
  - Advanced AIDS carries higher risk
Dental management

C. Complications:
- opportunistic infections, bleeding problems, hypotension, headache, fever, nausea, increased risk of NHL, Kaposi’s Sarcoma, Oral hairy leukoplakia, perio, ANUG/NUG, candida
- Advanced AIDS carries higher risk
Dental management

- D. Drugs:
  - Be aware of all drugs (antimicrobials, ARTs, dose, how long, how monitored, compliance, etc.)
  - Check drug interactions before prescribing. Some drugs may cause mucosal eruptions.
Dental management

- E. Emergency Treatment: no issues

- F. Follow up:
  - Stage 1 = Routine and periodic follow-up.
  - Stage 2-3 = more frequent follow-up or additional prophylactic agents
Dental management

- For a patient with HIV who is stable, well-controlled and monitored without severe infections or co-morbidities, dental treatment can be provided pretty much the same as for any patient.