LECTURER

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ORAL MANIFESTATIONS OF HIV/AIDS
Diagnostic and Treatment
SEVERE ACQUIRED IMMUNODEFICIENCY IN MALE HOMOSEXUALS, MANIFESTED BY CHRONIC PERIANAL ULCEERATIVE HERPES SIMPLEX LESIONS

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Abstract Four homosexual men presented with gradually enlarging perianal ulcers, from which herpes simplex virus was cultured. Each patient had a prolonged course characterized by weight loss, fever, and evidence of infection by other opportunistic microorganisms including cytomegalovirus, Pneumocystis carinii, and Candida albicans. Three patients died; Kaposi’s sarcoma developed in the fourth. All were found to have depressed cell-mediated immunity, as evidenced by skin anergy, lymphopenia, and poor or absent responses to plant lectins and antigens in vitro. Natural-killer-cell activity, directed against target cells infected with herpes simplex virus was depressed in all patients. The absence of a history of recurrent infections or of histologic evidence of lymphoproliferative or other neoplastic diseases suggests that the immune defects were acquired. (N Engl J Med. 1981. 305:1439-44.)
Summary of HIV cellular targets

- Malabsorption
- Weight loss
- Hypersecretion
- Diarrhoea
- AIDS

Intestinal cell

Lymphocyte CD4

Bone marrow

Progenitor CD34

Macrophage

Anemia

Lymphopenia

Thrombocytopenia

URRMA R&D
EPIDEMIOLOGY: 39,5 infected
HIV infection course

OUTLINE

• What are the factors affecting the occurrence of oral manifestations?
• What are the oral manifestations of HIV/AIDS?
• What effect has HAART had on oral manifestations?
• Do oral manifestations indicate seroconversion or progression to more severe immunosuppression?
• Are dental patients with HIV more prone to post operative complications?
• Are dentists exposed to aerosols at higher risk of contracting HIV?
• What is the newest HIV test?
NEW Classification of oral diseases of HIV – associated immune suppression (ODHIS) - 2004

- Past classification systems for HIV – associated oral lesions developed in the early 1990’s
- HAART (Antiretroviral drug therapy)
- Changing pattern of oral conditions
NEW Classification of oral diseases of HIV – associated immune suppression (ODHIS) - 2004

- **Group 1** – ODHIS associated with severe immune suppression (CD4<200 cells/mm³)
- **Group 2** – ODHIS associated with immune suppression (CD4<500 cells/mm³)
- **Group 3** – ODHIS assumed associated with immune suppression
  - **A)** More commonly observed
  - **B)** Rarely reported
- **Group 4** – Therapeutically-induced oral diseases
- **Group 5** – Emerging oral diseases
NEW Classification of oral diseases of HIV – associated immune suppression (ODHIS) - 2004

- Oral diseases do not belong exclusively to one classification Group

- Overlap may exist
Group 1. ODHIS associated with severe immune suppression (CD4<200 cells/mm3)

- Major recurrent aphthous ulcer
- Neutropenia - induced ulcers
- Necrotizing ulcerative periodontitis
- Necrotizing stomatitis
- Cytomegalovirus (CMV) lesions
- Chronic HSV
- Histoplasmosis lesions
- Esophageal, pseudomembranous, and hypertrophic candidiasis
- Oral hairy leukoplakia
- Kaposi’s sarcoma
Pseudomembranous Candidiasis
Esophageal Candidiasis
Hyperplastic Candidiasis
Pseudomembranous Candidiasis / KS
Kaposi’s Sarcoma
Kaposi’s Sarcoma
Histoplasmosis
Periodontitis
Idiopathic Necrotizing Stomatitis

- Consider:
  - Bacterial
  - Viral
  - Fungal
  - Combination
Necrotizing Stomatitis
 Chronic HSV
Oral Hairy Leukoplakia
Group 2. ODHIS associated with immune suppression (CD4,500 cells/mm3)

- Major recurrent aphthous ulcer
  (Increased frequency, harder to treat, atypical location)
- Salivary gland disease
  - Drug induced low salivation
  - Facial palsy
  - Neuropathies
- Erythematous candidiasis
- Hyposalivation
- Human papilloma virus (HPV)
- Linear gingival erythema
- Non-Hodgkin’s lymphoma
Aphthous Ulcer: Minor
Aphthous Ulcer: Major
Erythematous Candidiasis

ORAL MANIFESTATIONS OF HIV/AIDS

Diagnostic and Treatment
Linear Gingival Erythema
Human Papilloma Virus
Group 3. ODHIS assumed associated with immune suppression

- More commonly observed:
  - Angular candidiasis
  - Herpes labialis
  - Intra-oral herpes
  - Minor aphthous ulcers

- Rarely reported:
  - Bacillary epithelioid angiomatosis
  - Tuberculosis
  - Deep-seated mycosis (except histoplasmosis)
  - Molluscum contagiosum
  - Varicella Zoster Virus (VZV)
Angular cheilitis (Candida spp)
ORAL MANIFESTATIONS OF HIV/AIDS

Diagnostic and Treatment

HSV Labialis
Intra-oral Herpes
Miner Aphthous Ulcers
Coccidiomycosis
Group 4. Therapeutically-induced oral diseases

- Side-effect
  - Melanotic hyperpigmentation
  - Ulcers
  - Hyposalivation
  - Lichenoid drug reaction
  - Neutropenia - induced ulcers

- Thrombocytopenia
- Lipodystrophy-associated oral changes
- Perioral paresthesia
- Steven Johnson’s?
- Exfoliative cheilitis?
Group 4. Therapeutically-induced oral diseases

- Resistance-induced diseases:
  - Different Candida spp and strains
  - HSV
Antiretroviral drugs and Adverse Reactions

- **Drugs**
  - Indinavir
  - Saquinavir
  - Amprenavir
  - Nevirapine
  - Delavirdine
  - Efavirenz
  - Stavudine
  - Didanosine

- **Adverse reactions**
  - Oral ulcers
  - Stevens Johnson’s
  - Taste changes
  - Dryness
  - Perioral paresthesia
  - Thrombocytopenia
Ulcers – Medication Induced

Recurrent HSV
Group 5. Emerging oral diseases

- Human papilloma virus, several HPV types (may be associated with immune reconstitution)
- Erythema migrans
- Variants of Non-Hodgkin’s Lymphoma (NHL B-cell types)
- Epithelial neoplasms
- Aggressive interproximal dental caries
Oral squamous papilloma.
Condyloma Accuminatum

HPV Genotypes 6 & 11
Squamous Cell Carcinoma
WHAT EFFECT HAS HAART HAD ON ORAL MANIFESTATIONS?

- Significant reduction – oral hairy leukoplakia, necrotizing ulcerative periodontitis, Kaposi’s sarcoma

- No significant reduction – candidiasis, oral ulcers,

- Increase – salivary gland disease, oral warts, caries

- Reduction of oral lesions - 47.6% to 37.5%
Aggressive Interproximal Caries
DO ORAL MANIFESTATIONS INDICATE SEROCONVERSION OR PROGRESSION TO MORE SEVERE IMMUNOSUPPRESSION?

• Kaposi’s sarcoma may be an indicator of progression to severe immunosuppression
ARE DENTIST EXPOSED TO AEROSOLS AT HIGHER RISK OF CONTRACTING HIV?

- Transmission via aerosols has not been documented
ARE DENTAL PATIENTS WITH HIV MORE PRONE TO POST OPERATIVE COMPLICATIONS?

• YES and NO!
WHAT IS THE NEWEST HIV TEST?

- OraQuick rapid HIV test for oral fluid
Oral Health Management for the HIV/AIDS Patient
Medical Management of HIV

- **Opportunistic Infection Prophylaxis**
  - recurrent Candida = fluconazole, clotrimazole
  - recurrent HSV = acyclovir
  - TB (if PPD+) = INH + B₆, RIF + PZA
  - PCP (CD4 < 200) = TMP-SMX, dapsone
  - Toxo (CD4 < 100) = TMP-SMX, dapsone
  - MAC (CD4 < 75) = azithromycin, clarithromycin

- **Antiretroviral Therapy (HAART)**
  - 3 – 4 anti-HIV meds used in a combination regimen
Antiretroviral Agents

- **Nucleoside Analog RT Inhibitors (NRTIs)**
  - **Thymidine:** AZT / ZDV = zidovudine = Retrovir
    - d4T = stavudine = Zerit
  - **Adenosine:** ddI = didanosine = Videx
    - TFV = tenofovir = Viread
  - **Cytidine:** 3TC = lamivudine = Epivir
    - ddC = zalcitabine = Hivid
  - **Guanosine:** ABC = abacavir = Ziagen
    - ZDV+3TC = dual NRTI = Combivir
    - ZDV+3TC+ABC = triple NRTI = Trizivir

ORAL MANIFESTATIONS OF HIV/AIDS
Diagnostic and Treatment
### Antiretroviral Agents

**Non-nucleoside RTIs**
- Nevirapine = *Viramune*
- Delavirdine = *Rescriptor*
- Efavirenz = *Sustiva*

**Protease Inhibitors**
- Indinavir = *Crixivan*
- Nelfinavir = *Viracept*
- Ritonavir = *Norvir*
- Saquinavir = *Fortovase* = *Invirase*
- Amprenavir = *Agenerase*
- Lopinavir/Ritonavir = *Kaletra*

- **Fusion Inhibitor**
- Enfuvirtide (T-20)
Role of Oral Health Professionals in HIV Care

- Provide preventive and therapeutic dental care to improve health and reduce complications from dental infections
- Help maintain overall physical well-being of patients and improve health outcomes
- Recognize, treat, and understand the significance of oral lesions
Routine Oral Care of HIV Patients

- Is part of a multidisciplinary approach by improving oral health and maintaining overall health
- Recognize oral manifestation of systemic disease – diabetes, HIV, eating disorders...
- Is usually straightforward and requires no special facility or equipment
- Clinicians should comply with the current infection control recommendations
Assessment of HIV Patients

- The medical complexities of patients with HIV often involve non-HIV associated conditions
  - diabetes, heart, liver & kidney diseases, etc
- Develop an appropriate dental treatment plan:
  - Assess patient’s overall health (not just HIV issues) and screen for underlying medical conditions that may require modification of dental care
  - Obtain a medical history and labs in consultation with the patient’s primary provider
  - Assess risks associated with dental care
Medical History & Labs

- CBC with differential
- PT, PTT, INR, hemoglobin and neutrophils
- CD4 cells and Viral load
  - first count; lowest count; latest count
- Recent HIV-related symptoms or illnesses
- HAV/HBV/HCV and TB status
- Current medications
Assessment of the Risks Associated with the Provision of Dental Care

- **Hemostasis**
  - Clotting factors are decreased in severe liver disease
  - Number & function of platelets may be reduced and factor replacement or transfusion may be required
  - Need PT/PTT for patient within 48 hrs of surgery
  - Elective surgery can be safely performed in pts with platelets >60,000/mm³ and PT/PTT of 0.8-2.5 INR
  - For multiple extractions / extensive cleaning, remove 1 tooth or clean 1 area at a time and then proceed
Assessment of the Risks Associated with the Provision of Dental Care

- **Susceptibility to infections**
  - low CD4 count, leukopenia, neutropenia
  - hyperglycemia and diabetes
  - other immuno-compromised conditions

- **Drug actions and interactions**
  - polypharmacopoeia: HIV-related and other meds
  - antibiotics (prophylaxis, etc): avoid “doubling up”
  - hepatic and/or renal disease
# Laboratory Values

(Reznik and Bednarsh, June 2006)

## Table 1. Pertinent Laboratory Information

<table>
<thead>
<tr>
<th>Lab Values</th>
<th>Normal, Male</th>
<th>Normal, Female</th>
<th>Abnormal Values of Importance</th>
<th>Impact on the Provision of Invasive Dental Care</th>
<th>Need to Premedicate</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 count</td>
<td>400 – 1,200 cells/mm³</td>
<td>500 – 1,600 cells/mm³</td>
<td>&lt; 200 cells/mm³ is an AIDS defining condition</td>
<td>None</td>
<td>No</td>
</tr>
<tr>
<td>HIV viral load</td>
<td>Undetectable</td>
<td>Undetectable</td>
<td>40 copies/mL, &lt;750,000 copies/mL</td>
<td>None, even at the highest levels</td>
<td>No</td>
</tr>
<tr>
<td>Platelet count</td>
<td>150,000 – 450,000 per microliter (mcl) of blood</td>
<td></td>
<td>&lt; 20,000 platelets/mcl may lead to spontaneous bleeding</td>
<td>Dental procedures can safely be performed with a platelet count of 60,000 mcl or greater.</td>
<td>No</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>14.0 g/dL – 17.4 g/dL (nonpregnant women)</td>
<td>12.3 g/dL – 15.3 g/dL</td>
<td>Anemia in men &lt;13 g/dL Anemia in women &lt; 12/dL</td>
<td>Periodontal and minor surgical procedures (eg, single extraction) are usually routine for patients with hemoglobin level above 7 g/dL and no bleeding abnormalities</td>
<td>No</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>40% - 52%</td>
<td>35% - 47%</td>
<td>Values that fall below the normal limit indicate anemia</td>
<td>Monitor hematocrit as excessively low values may indicate severe anemia</td>
<td>No</td>
</tr>
<tr>
<td>White blood cell count/absolute neutrophil count (ANC)</td>
<td>4,500 – 10,000 white blood cells/mcl</td>
<td></td>
<td>&lt; 1,000 white blood cells/mcl</td>
<td>May signify low absolute neutrophil count. An absolute neutrophil count &lt;500 cells/mcl requires premedication prior to invasive dental procedures.</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Note: Normal lab values obtained from Medline Plus, a service of the National Institutes of Health.
Aggressive Prevention Efforts

- Recall visits every 3 – 4 months
- BWX every 6 – 8 months
- Topical fluoride foam or varnish
- Assess need for oral hygiene instruction and dispense toothbrush, other aids, antimicrobials
- Nutritional counseling
Cavity Prevention

- Toothpaste & floss
- Proxabrush
- Rinses
Xerostomia Aids

- Rx fluoride paste
- Mouth spray
- Xylitol-based gum
Routine Oral Care of HIV Patients

Treat as indicated:

- **Restorative**
  - same

- **Oral Surgical Procedures**
  - Take care to minimize bleeding and trauma, postoperative complications no higher than in the HIV-negative group

- **Removable Prosthodontics**
  - same
Invasive Dental Procedures

- Follow aseptic technique
- Have results of recent labs to assess hemostatic function and susceptibility to infection
- Incidence of post-procedure complications is no greater than other populations (w/o diabetes), although patients with prolonged clotting time will experience delayed wound healing
Indications for Antibiotic Prophylaxis

- Literature does not support routine antibiotic prophylaxis, decision to use antibiotic should be made on an individual basis
- If Neutrophil count is <500 cells/mm3, antibiotic use indicated.
- Ask specifically about hospitalizations due to bacterimia (esp. in the IDU population) and consult with PCP
- Follow the updated AHA guidelines on antibiotic prophylaxis to prevent bacterial endocarditis
Indications for Antibiotic Prophylaxis

- CD4 count is **not in itself** an indication for prophylaxis, but patients with CD4 <100 or on long-term chemotherapy should be checked for neutropenia.
- For moderate neutropenia (absolute count 500-1000), determine antibiotic use based on procedure performed (if extensive prophylaxis), anticipated risk of secondary infection, and consultation with physician.
- For severe neutropenia (absolute count <500) antibiotics should be used before all invasive dental procedures.
- Preferred prophylaxis: AHA antibiotic prophylaxis regimen prior to invasive dental procedure.
Candidiasis Treatment

- Topical therapy with nystatin or clotrimazole; tx length is usually 10-14 days, follow-up in 2 wks
- Clotrimazole 10mg, 1 tab 5x/day, dissolve slowly and swallow, 10 day treatment
- For oropharyngeal/esophageal disease, apply systemic treatment with fluconazole 100 mg/day for 10 days, follow-up in 2 wks
Bacterial Diseases

- Linear Gingival Erythema
- Necrotizing Ulcerative Gingivitis
- Necrotizing Ulcerative Periodontitis
Linear Gingival Erythema

- profound erythema of the free gingival margin, responds poorly to treatment, usually asymptomatic.
- treatment = plaque removal and reinforce good oral hygiene, follow-up in 2 wks, frequent recalls, chlorhexadine
Necrotizing Ulcerative Gingivitis

- Erythema with mild ulceration of gingival tissue
- Treatment is usually very successful
  - aggressive plaque removal
  - Thought to be a precursor of the more extensive ulcerative periodontitis
  - follow-up in 3-4 days; dental visits every 3-4 mos for cleaning
  - stress good oral hygiene and return for any recurrence of sx.
Necrotizing Ulcerative Periodontitis

- Erythema with ulceration and loss of interdental papillae, necrotic tissue and bone, halitosis, severe pain and loose teeth

- Treatment is usually very successful
  - aggressive plaque removal (may need to numb up first)
  - debridement of necrotic tissue and chlorhexadine rinsing (with add’l use of metronidazole if large areas are affected)
  - follow-up in 3-4 days; dental visits every 3-4 mos for cleaning
  - stress good oral hygiene and return for any recurrence of sx$s$. 
Viral Diseases

- Hairy Leukoplakia
- Herpes Simplex
- Human Papilloma Virus (HPV)
- Kaposi Sarcoma
- Cytomegalovirus
Hairy Leukoplakia

- Bilateral symmetrical white corrugated lesions on the lateral borders of the tongue as a result of reactivation of EBV
- Usually asymptomatic, requires no treatment but podophyllum resin peels may be used
- DD = tobacco associated leukoplakia, lichen planus, epithelial dysplasia, hyperplastic candidiasis
Herpes Simplex

- One or more lesions usually on keratinized mucosa, hard palate, gingiva but may also be on vermillion border of lips and adjacent facial skin
- Begins as painful multiple lesions and may coalesce into large, erosive ulceration
- Treat with oral acyclovir for 10-14 days, follow up in 2 wks
Oral HPV Infection

- Exophytic papillary lesions with cauliflower-like surface to raised, flat, or smooth lesions; solitary or multiple

- Treatment:
  - Excision (for small lesions)
  - Cryotherapy
  - CO2 laser ablation (in-hospital)
  - Interferon-alpha (intra-lesional)
Aphthous Ulceration

- Unknown etiology (trauma, hormones, meds?)
- Non-keratinized mucosa, cheeks, lips, soft palate, floor of mouth, ventral tongue

- Minor: < 1cm, self-limiting, minor discomfort
  \[ Tx = \text{topical steroid and/or anesthetic, f/u in 10-14 days} \]

- Major: > 1cm, deep into connective tissue, dysphagia
  \[ Tx = \text{systemic steroids (prednisone, 80mg/day x 7 days)} \]
  Alternative tx = thalidimide
HIV Salivary Gland Disease

- Recurrent or persistent major salivary gland enlargement and xerostomia
- Treat associated xerostomia with pilocarpine (5mg TID) or other meds to increase secretion, sugarless chewing gum, sugarless lemon drops, topical fluoride and frequent dental cleanings
Xerostomia

- Up to 30% of patients taking didanosine and 7% of patients using protease inhibitors may experience xerostomia
- Minimize use of alcohol and alcohol based mouthwashes
- Drink more water, sugarless chewing gums, xylitol based gums
- At home use of fluoridated pastes and gels
Long Term Effects of Xerostomia

- Salivary Gland Enlargement
- Oral Mucosal Soreness
- Dry, sore, cracked lips
- Oral Candidiasis
- Increased frequency of cervical caries
- Gingival and periodontal disease
- Depapillation of tongue (burning tongue)
- Trouble eating, swallowing and speaking
- Dysgeusia (bad taste)
Clinical Care

- Initial treatment plan should include prophylaxis, fluoride treatment and caries control to determine tooth restorability
- In office and home use of fluorides, OHI, increase/stimulate salivary: switch to water, sugarless gum, pilocarpine, review OHI.
- Damage to teeth is so extensive that the only option is extraction and fabrication of dentures