

HIV and Oral Health 101

Part 3: Oral Manifestations in the Era of Antiretroviral Therapy

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Disclosures

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- **The speakers will not discuss any off-label use or investigational product during the program.**
- **This slide set has been peer-reviewed to ensure that there are no conflicts of interest represented in the presentation**
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Objectives



- **Understand the change in oral health needs in the Era of ART therapy**
- **Evaluate common oral manifestations related to HIV**
- **Understand current therapies for oral conditions**

Oral Health and HIV

- 90% of PLWHA have a chronic oral condition
- 32-46 percent of PLWHA will have at least one major HIV-related oral health problem.
- 58-68 percent PLWHA do not receive regular health care.
- Barriers PLWHA face in receiving oral health care include lack of insurance, limited incomes, lack of providers, stigma, and limited awareness.
- Poor oral health can impede food intake and nutrition, leading to poor absorption of HIV medications and leaving PLWHA susceptible to progression of their disease.
- HIV medications have side effects such as dry mouth, which predisposes PLWHA to dental decay, periodontal disease, and fungal infections.

http://hthab.hrsa.gov/aboutab/files/oral_health_fact_sheet.pdf

Oral Health and HIV

- Bacterial infections (i.e., dental decay and periodontal disease) that begin in the mouth can escalate to systemic infections and harm the heart and other organs if not treated, particularly in PLWHA with severely compromised immune systems.
- A history of chronic periodontal disease can disrupt diabetic control and lead to a significant increase in the risk of delivering preterm low-birthweight babies.
- Poor oral health can adversely affect quality of life and limit career opportunities and social contact as result of facial appearance and odor.

http://hab.hrsa.gov/abouthab/files/oral_health_fact_sheet.pdf

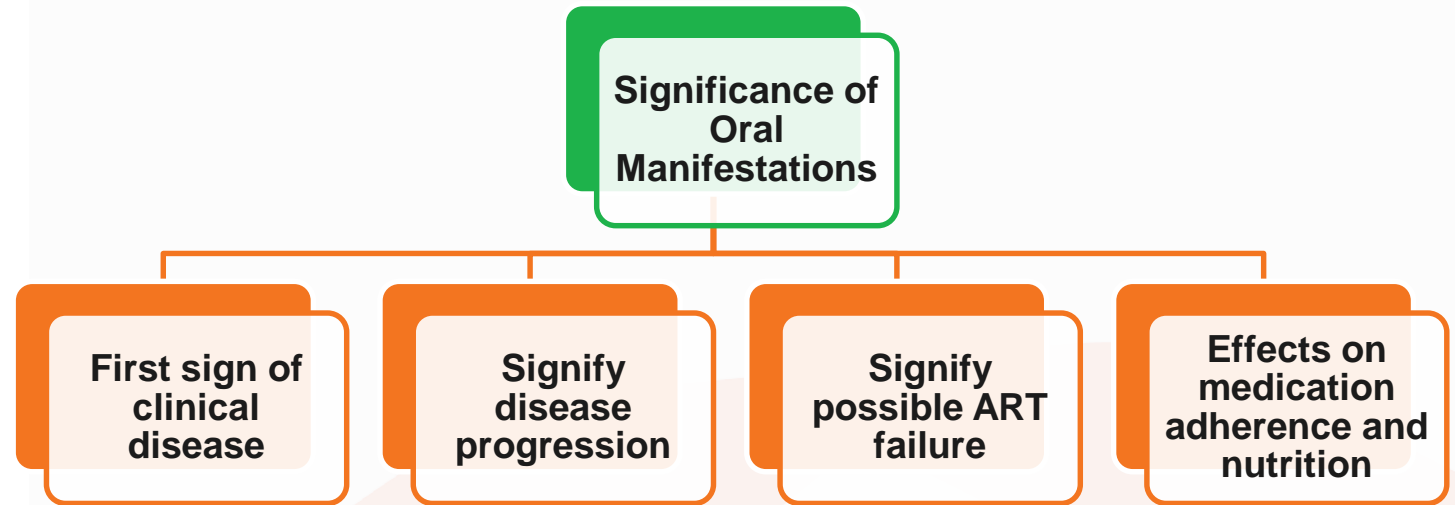
Oral Health and HIV

HAB's (HIV AIDS Bureau) Oral Health Performance Measures

- **Dental and medical history**
- **Dental treatment plan oral health education**
- **Periodontal screening or examination**
- **Phase I treatment plan completion (prevention, maintenance, elimination of oral health disease)**

http://hab.hrsa.gov/abouthab/files/oral_health_fact_sheet.pdf

Oral Manifestations of HIV





Oral Manifestations of HIV

In the Era of ART

Decreasing:

- Candidiasis
- Necrotizing Gingivitis
- Kaposi's Sarcoma
- Oral Hairy Leukoplakia

Increasing:

- Dental Decay/Periodontal Disease
- Oral HPV



XEROSTOMIA



There are multiple causes of xerostomia:

- Anticholinergic effects of many medications**
- Alcohol and drug abuse**
- Damaging head and neck radiation**
- Comorbidities from HIV/AIDS such as cardiac disease, diabetes, and mental health disorders which occurs in PLWHA. As a result, many of the medications especially the antidepressants, anxiolytics, diuretics, and antihistamines being taken for these comorbidities**
- There are still differing studies of the xerostomic effects of antiretroviral medications used to treat HIV.**

Xerostomia is the subjective complaint of oral dryness. This must be distinguished from salivary gland dysfunction which is an objective disease characterized by reduced salivary flow. Studies have shown that 40% or more of PLWHA experience major xerostomia during their disease. Studies of PLWHA with xerostomia show a frequently negative effect on their quality of life.

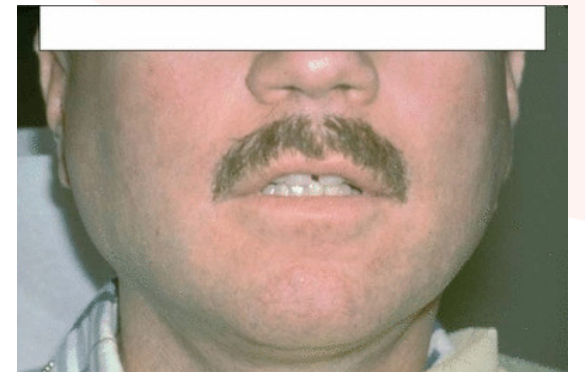
Symptoms of xerostomia include cracked peeled atrophic lips, glossitis, and pale dry buccal mucosa. Xerostomia can lead to dysphagia, oral pain of unknown origin, dental caries, oral infections, periodontal disease, angular cheilitis associated with candidiasis and can affect the health-related quality of life. These features of xerostomia can lead to the inability of the patient to take necessary medications, and can influence intake of proper nutrients, leading to malnutrition and a decline in overall health.



More significant in the era of ART is the increase in prevalence of salivary gland disease. Salivary gland disease can arise in 4% to 10% of adults and children with HIV.

HIV salivary gland disease (HIV-SGD) is a distinct disorder characterized by persistent major salivary gland swelling and xerostomia. Most commonly affected is one or both parotid glands sometimes which will occur without xerostomia. In some cases, salivary gland enlargement may be the first clinical manifestation of HIV infection, but more often a sign of late HIV infection.

The exact pathophysiology of HIV-SD, origins include lymphoepithelial lesions, cysts, intraglandular lymph nodes, and an inflammatory infiltrate similar to what is often observed in Sjogren's, syndrome however with distinct histopathologic and serological differences. In the infiltrate, there are persistent circulating CD8+lymphocytosis and diffuse visceral CD8+ lymphocytic infiltration.



Treatment for Xerostomia

Salivary stimulants such as sugarless gum or sugarless candies may provide relief.

Candies that are acidic should be avoided as frequent use may lead to loss of tooth enamel

Biotene, Eclipse, Extra, Orbit

Salivary substitutes

Biotene Oral Balance, Biotene Moisturizing Mouth Spray

Salivart (Xenex), Oralube(Xenex), Xerolube Colgate), Plax (Pfizer)

Pharmacologic Stimulants

Pilocarpine HCl ,Cevimeline HCl (Caution with Beta Blockers)

An increase in caries can occur, so fluoride rinses (that can be bought over the counter) or prescription fluorides should be used daily, and visits to the dentist should occur two to three times per year.

Treatment for Xerostomia

OTC products (.05% NaF) ACT, Fluoroguard

Prescription products

Prevident 5000 plus toothpaste/gel/rinse, Fluoride Varnish

Home Care Instructions

Brush, Floss, Tongue Scraper

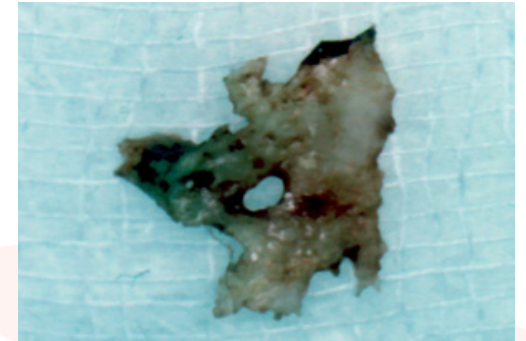
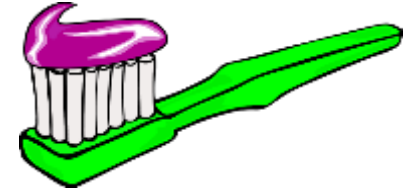
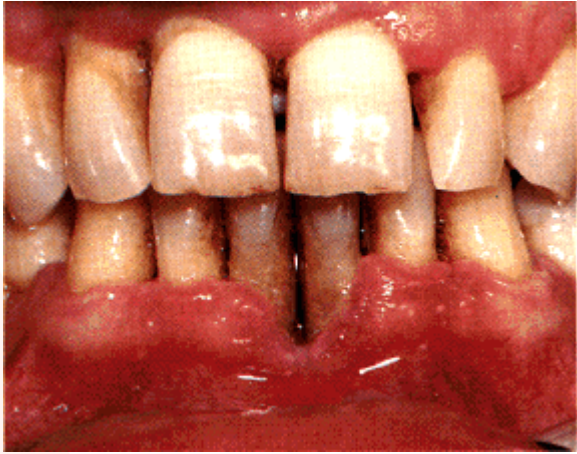
Dental Decay

Factors that Increase Dental Decay

- Xerostomia is moderate to severe in 30-40% living with HIV/AIDS
- Xerostomia is caused by many medications use to treat HIV and comorbidities related to both HIV and aging
- In addition the HIV virus effects the salivary glands can lead to salivary gland deformities and damages that also decrease salivary flow.
- Diet
- Substance Abuse
- Increased Life Expectancy



Periodontal Disease



Links between Periodontal Disease and other disease states/Diabetes/Heart Disease/Stroke

Periodontal Disease in the Era of ART

- **Shift of prevalence towards periodontal diseases.**
- **Lack of oral hygiene determined by plaque formation and reduced CD4-counts with pronounced periodontal inflammation can be seen as risk factors for periodontal disease. There is an increase in periodontal inflammation markers in patients with HIV.**
- **Increased prevalence of periodontal diseases in HIV-infected patients on antiretroviral therapy.**
- **Overall high prevalence of manifestations underlines the importance of oral examination for the general practitioner and visits by oral specialists should become a routine procedure in HIV-patients care.**

[Kroidl A¹](#), [Schaeben A](#), [Oette M](#), [Wettstein M](#), [Herfordt A](#), [Häussinger D](#). [Eur J Med Res](#). 2005 Oct 18;10(10):448-53

Periodontal Disease

Linear Erythematous Gingivitis This entity appears as a 1 -3mm band of marginal gingival erythema, often with petechiae. It is typically associated with no symptoms or only mild gingival bleeding and mild pain.

Histological examination reveals an incomplete or aborted inflammatory response with principally hyperemia present.

Oral rinsing with chlorhexidine gluconate 0.12% often reduces or eliminates the erythema and typically requires prophylactic use to avoid recurrence



What can we do?

■ Periodontal Disease

- Amoxicillin 250mg 3 x/day with Metronidazole 250mg 3X/day x 5-7days
- Antimicrobial rinses (0.12% Chlorhexidine) 15cc 2xday x 14days
- Concurrent Antifungal maybe necessary
- Referral for immediate dental care
- Stress oral home care for clients and routine dental care

- **Oral candidiasis and oral hairy leukoplakia appear to be the first and the second most common oral opportunistic infections associated with HIV.**

S Sethi, [DN Kiran](#), [G Popli](#), A Malhotra, A Bansal... - 2016 - recentscientific.com

Oropharyngeal Candidiasis (OPC)

- The most common HIV related oral lesion is Candidiasis,
- predominantly due to infection by *Candida albicans*.

- Non albicans species such as *C. glabrata*, *C. tropicalis*, *C. krusei* and *C. kefyr* have been reported in 1% to 20% of HIV infected patients.

- It is often the initial manifestation of symptomatic infection with
- HIV, and may simply imply concurrent esophageal candidiasis, which is an AIDS indicator lesion, or also be a predictor of the likelihood of other opportunistic infections.

Baccaglini L, Atkinson JC, Patton LL, Glick M, Ficarra G, Perterson DE. Management of oral lesions in HIV positive patients. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103(suppl1):s50.e1

Oropharyngeal Candidiasis (OPC)

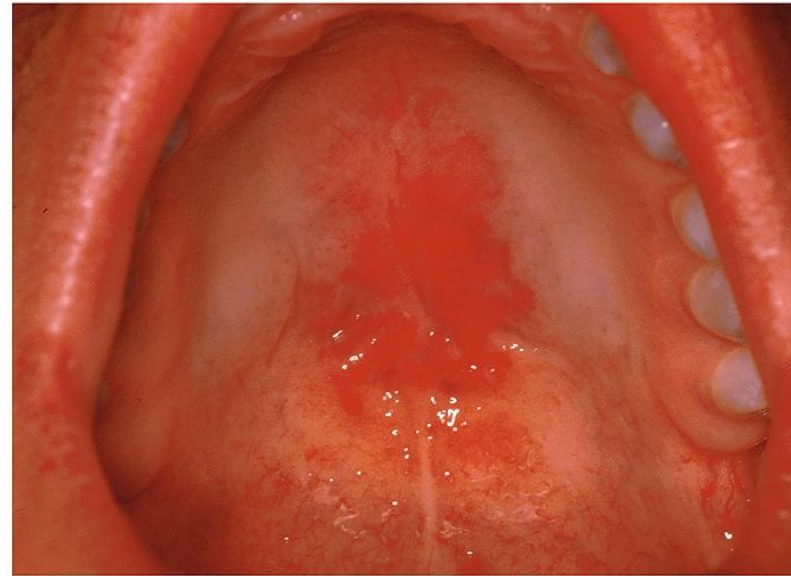
- **Pseudomembranous candidiasis: Acknowledged as the most common variant, it presents as creamy, white, curd like plaques on the oral mucosa or tongue which can be wiped away, leaving a red erythematous surface. Patients may complain of soreness or burning in the mouth**



Baccaglini L, Atkinson JC, Patton LL, Glick M, Ficarra G, Perterson DE. Management of oral lesions in HIV positive patients. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103(suppl1):s50.e1

Oropharyngeal Candidiasis (OPC)

- **Erythematous candidiasis:** It presents as a red, flat, subtle lesion on the dorsum of tongue. A kissing lesion occurs when the lesion present on the tongue has a matching counterpart on the hard or soft palate where it comes in contact. The lesion is often symptomatic, with burning mouth sensations.



<https://images.search.yahoo.com/yhs/search?p=erthematgous+candidiasis&fr=yhs-mozilla-003&hspart=mozilla&hsimp=yhs->

Oropharyngeal Candidiasis (OPC)

- **Hypertrophic Candidiasis:** Thick white plaques that cannot be readily removed may indicate the presence of hyperplastic candidiasis. This may occur concurrently with oral hairy leukoplakia.
- **Angular Cheilitis:** It presents as cracking, fissuring, ulceration or erythema of the corners of the mouth, and may occur with or without the presence of erythematous or pseudomembranous candidiasis. It tends to persist for long periods of time without treatment.



https://images.search.yahoo.com/yhs/search;_ylt=A0LEVvwnCO1YGyoAzTwnnllQ?p=angular+cheilitis+candidiasis

Oropharyngeal Candidiasis (OPC)

- **Early treatment of oral candidiasis is warranted not only because of the discomfort caused by the lesions, but also because the foci may act as reservoirs of organisms for local spread of disease.**
- **It takes longer to eradicate candidiasis in HIV infected population, and relapse rates are high.**
- **High fungal counts and smoking appear to increase the tendency for poor response.**
- **Use of topical agents for treatment of OPC is recommended as initial therapy, more so owing to concerns of drug interactions between systemic antifungals and antiretroviral therapy.**

Oral manifestations of HIV infection and their management. I. More common lesions. Oral Surg
Oral Med Oral Pathol 1991;71:158

Oropharyngeal Candidiasis (OPC) Treatment

Topical antifungal agents include nystatin, clotrimazole, amphotericin B which can be delivered as oral suspensions, troches or tablets. Systemic therapy with ketoconazole, fluconazole, or Itraconazole is indicated in recurrent cases.

Recommend 200mg once daily oral dose of Nizoral (ketoconazole) for resolution of oral signs and symptoms. Although fluconazole is an effective mucosal antifungal drug, candidal recurrence and resistance to fluconazole appear to be an emerging problem.

Oral Hairy Leukoplakia

Hairy leukoplakia (also known as oral hairy leukoplakia, or HIV-associated hairy leukoplakia), is a white patch on the side of the tongue with a corrugated or hairy appearance. It is caused by Epstein-Barr virus (EBV) and occurs usually in persons who are immunocompromised especially those with HIV/AIDS). This white lesion cannot be scraped off. The lesion itself is benign and does not require any treatment, although its appearance may have diagnostic and prognostic implications for the underlying condition.

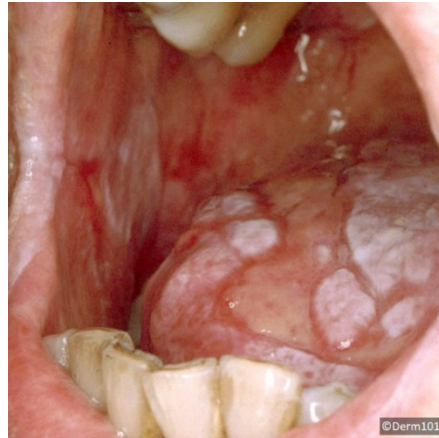


<http://diseasespictures.com/oral-hairy-leukoplakia>

Walling DM 2003 (PMID 12964120) Moura MD 2010 (PMID 20813564)

Oral Hairy Leukoplakia

Treatment is not necessary since the lesion is benign, however the person may have esthetic concerns about the appearance. The condition often resolves rapidly with high dose acyclovir or desiclovir but recurs once this therapy is stopped, or as the underlying immunocompromised condition worsens. Topical use of podophyllum resin or retinoid as also been reported to produce temporary remission. Antiretroviral drugs such as zidovudine may be effective in producing a significant regression of OHL. Recurrence of the lesion may also signify that ART is becoming ineffective.



<http://diseasespictures.com/oral-hairy-leukoplakia>

Walling DM 2003 (PMID 12964120) Moura MD 2010 (PMID 20813564)

Herpes Simplex (HSV) Viral Lesions



<http://medicalpicturesinfo.com/herpes-simplex/>



<https://www.dermquest.com/image-library/image/5044bfcfc97267166cd62bab>

<http://gr.dentistbd.com/primary-herpetic-gingivostomatitis-ppt.html>

Herpes Simplex (HSV)

- HSV infection in healthy individuals characteristically presents
 - with cold sores on the vermillion border of the lips, or small shallow ulcers with irregular white borders or vesicles on keratinized oral tissues.
 - Lesions in HIV infected population:
 - often occur as ulcers on the non-keratinized tissues such as labial mucosa, buccal mucosa, ventral tongue, and soft palate. Such ulcers are extremely painful, may be clustered or coalescent, or present as a discrete large ulcer mimicking and aphthous ulcer.
 - 28% incidence of co-infection with cytomegalovirus (CMV)
- Diagnosis
 - Lab Testing is recommended HSV DNA PCR or viral culture and antigen detection

Herpes Simplex (HSV)

Treatment

- **Oral Valacyclovir, Famciclovir, or Acyclovir for 5 to 10 days. Intravenous Acyclovir may be required for severe mucocutaneous disease**
- **Patients may opt for episodic treatment or for daily suppressive therapy if they experience frequent or severe outbreaks.**
- **Long term suppressive therapy reduces the number of recurrences of mucocutaneous HSV disease in HIV-infected patients. Acyclovir 400 mg twice daily, Famciclovir 500 mg twice daily, and Valacyclovir 500 mg twice daily are recommended options for chronic suppressive therapy in HIV-infected patients.**

Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf

Apthous Ulcers



medicalpicturesinfo.com/apthous-ulcers

Apthous Ulcers

- **Apthous ulcers (also called apthous stomatitis) affect up to 15% of HIV-infected patients**
- **Patients with HIV typically have oral ulcers that are more extensive, more frequent in occurrence, and slower to heal.**
- **Cause unknown**

Diagnosis

- **Diagnosis of apthous stomatitis is based on clinical presentation**
- **Exclusion of other possible causes, including HSV, syphilis, neoplasm, or drug reaction**

Greenspan D 2001 (PMID 11356441)

Aphthous Ulcers

Treatment

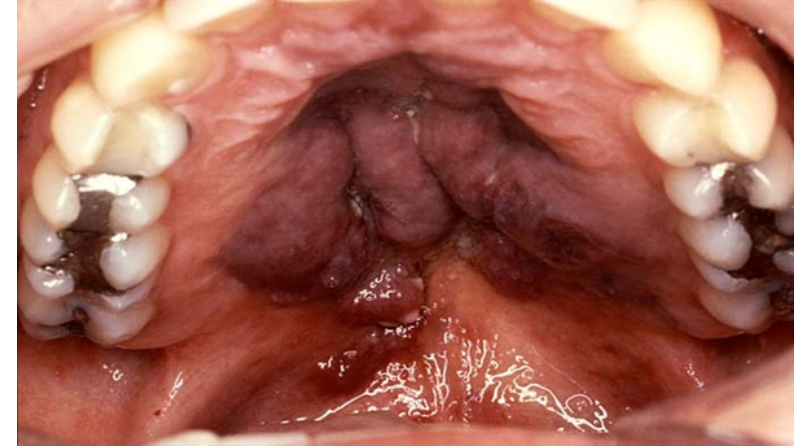
- **Topical anesthetics**
- **Topical corticosteroid, ideally combined in a dental paste preparation**
- **Severe lesions may require systemic or intraregional corticosteroids, or the immunomodulatory, thalidomide**
- **Antiretroviral therapy is a critical component in treating aphthous stomatitis**
- **Vitamin B12**
- **Topical tetracycline's may reduce the severity of ulceration, but they do not alter the recurrence rate. A doxycycline capsule of 100 mg in 10 mL of water administered as a mouth rinse for 3 minutes or tetracycline 500 mg plus nicotinamide 500 mg administered 4 times daily may provide relief and reduce ulcer duration.**

Baccaglioni L 2011 *Oral Dis.* Nov 2011; 17(8):755-70. Brocklehurst P 2012

Kaposi's Sarcoma



<http://www.netce.com/coursecontent.php?courseid=897>



<http://www.oncologynurseadvisor.com/kaposi-sarcoma-of-the-mouth/slideshow/952>

Squamous Cell Carcinoma



https://images.search.yahoo.com/yhs/search;_ylt=A0LEVicEHe1Y_TYAzO8nnIIQ?p=oral+cancer+squamo

Pain Syndromes

- **Pain is a common symptom experienced by patients with HIV infection. It may result from a wide variety of diseases including direct effects of HIV on central or peripheral nervous system, infection, malignancy or ART. Headache is a common symptom, occurring in approximately 46% patients with HIV infection.**
- **Neuropathic pain is common in patients with HIV infection, the most common diagnosis being painful peripheral sensory neuropathy**

Sirois DA. Oral manifestations of HIV disease. The Mount Sinai Journal of Medicine
1998;65(5&6):322-32

- **Combination ART has been documented to play a critical role in the prevention of oral manifestations of HIV because of its role in the reconstitution of the immune system.**
- **The escalating number of patients infected with HIV and the resulting cases of AIDS has produced an increased observation of oral manifestations associated with this syndrome.**
- **Thus, in addition to comprehensive general health care, oral health care is integral in the management of patients with HIV infection.**
- **The need is comprehensive quality dental care in a multidisciplinary setting with medical and social support providers as poor oral health care in these patients can complicate the management of systemic conditions, lead to nutritional deficiencies, affect antiretroviral treatment compliance and adversely affect quality of life.**

Risk Factors for Oral Lesions

- **Moderate and severe degrees of immunodeficiency and detectable viral loads were risk factors for the onset of oral lesions, irrespective of the use of ART.**
- **A mild immunologic impairment (CD4+ 350 to 500 cells/mm³) was sufficient to increase the risk of developing Hairy Leukoplakia nearly 11-fold and shows that immunologic deficiency could be considered to be an independently associated risk factor for the onset of these lesions.**
- **A detectable VL (> 50 copies/mm³) was a risk factor for Oral Candidiasis compared with undetectable circulating HIV-RNA. When this association is investigated together with CD4+ counts and use of ART in detectable VL did not augment the susceptibility of developing this fungal infection**

[Risk factors of HIV-related oral lesions in adults](#)

MNMR Petruzzi, [K Cherubini](#), [FG Salum](#)... - Revista de Saúde ..., 2013 - SciELO Public Health

Risk Factors for Oral Lesions

- **The components of cigarette smoke may induce chronic inflammation on the oral mucosae, cause damage to the innate immunity mechanisms against pathogens and inhibit cell growth by apoptosis mechanisms. These effects of smoking reduce the production of salivary enzymes and immunoglobulins and affect the production of lymphocytes, resulting in an imbalance of the oral microflora. These modifications probably encourage EBV infectivity, promoting the occurrence of Oral Hairy Leukoplakia.**
- **Smoking and alcohol consumption contributed to a high susceptibility to the development of these affections in the evaluated subjects.**

[Risk factors of HIV-related oral lesions in adults](#)

MNMR Petruzzi, [K Cherubini](#), [FG Salum](#)... - Revista de Saúde ..., 2013 - SciELO Public Health





Thank you

- ▶ We are available for clinical consultations and trainings