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REVIEW ARTICLE

ORAL MANIFESTATIONS OF HIV AND ITS MANAGEMENT- A REVIEW

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ABSTRACT

This paper discusses the importance of oral lesions as indicators of infection with human immunodeficiency virus (HIV) and as predictors of progression of HIV disease to acquired immunodeficiency syndrome (AIDS). Oral manifestation is among earliest the most important indicators of infection. Seven cardinal lesions oral candidiasis, hairy leukoplakia, Kaposi's sarcoma, linear gingival erythema, necrotising ulcerative gingivitis, necrotising ulcerative Periodontitis and non-Hodgkin's lymphoma, which are strongly associated with HIV infection, have been identified and internationally calibrated and are seen in both developed and developing countries. They may provide a strong indication of HIV infection and be present in the majority of HIV infected people. Antiretroviral therapy may affect the prevalence of HIV-related lesions. The presence of oral lesions can have a significant impact on health-related quality of life. Oral health needs in people with HIV infection, especially in children, and in adults particularly in medical programmes and to integrate oral health care with general care of the patient. It is important that all the health care workers receive education and training on the relevance of oral health needs and the use of oral lesions as surrogate markers.

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INTRODUCTION

Acquired immune deficiency syndrome (AIDS) was first reported in 1981 by Gottlieb et al at the University of California Medical Centre (Gottlieb *et al.,* 1981). In 1983, Barr'e – Sinoussiand Montagnier, isolated a new human T – lymphotrophic retrovirus, later named as human immunodeficiency virus type-1 (HIV-1) which turned out to be one of the causative agents of AIDS (Beena *et al.,* 2013). In September 1982 the CDC formally introduced the term Acquired Immunodeficiency Syndrome (AIDS) in describing the 593 cases reported to cause AIDS. Whereas the French team referred to the virus as Lymphadenopathy Associated Virus (LAV) and US team referred to the virus as Human T cell lymphotrophic virus type III (HTLV III). It became apparent that they were one and same (Burket's Oral Medicine). In May 1986, the unifying name of human immunodeficiency virus (HIV) was adopted by the International Committee on Taxonomy of viruses (Burket's Oral Medicine). Acquired Immunodeficiency Syndrome (AIDS) is caused by the Human Immunodeficiency Virus (HIV) and characterised by immunosuppression which leads to a spectrum of clinical manifestation that include opportunistic infections, secondary neoplasm and neurologic manifestation.

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Oral lesions can not only indicate infection with Human Immunodeficiency Virus (HIV), they are also among early clinical features of the infection and can predict progression of HIV disease to acquired immunodeficiency syndrome (AIDS). Oral manifestations are the earliest and most important indicators of HIV infection. (5-8)Seven cardinal lesions: oral candidiasis, hairy leukoplakia, Kaposi sarcoma, linear gingival erythema, necrotizing ulcerative gingivitis, necrotizing ulcerative periodontitis and non – Hodgkin lymphoma are strongly associated with HIV infection and have been identified internationally. These lesions may be present in up to 50% of people with HIV infection and in up to 80% of those with a diagnosis of AIDS (Palmer *et al.,* 1996). These oral lesions are usually clearly visible and can be diagnosed reliably from the clinical features alone (Greeanspan, 1997). These lesions parallel the decline in numbers of $CD4^+$ cells and an increase in viral load, and are independent indicators of disease progression (Greenspan, 2002).

Classification

Globally, the most widely used classification system for HIV oral lesions (HIV-OL) among adults and adolescents has been the HC-Clearinghouse on Oral Problems Related to HIV Infection and World Health Organisation (WHO) Collaborating Centre on Oral Manifestation of the Immunodeficiency Virus 1993 classification that outlined three groups (Patton *et al.,* 2013; Patton *et al.,* 2002) (Table 1, 2):

Table 1. September 1992 Consensus Classification of Oral Lesions Associated with Adult HIV Infection (EC-Clearinghouse, 1993)

Group I, Lesions strongly associated with HIV infection	Group II, Lesions less commonly associated with HIV infection	Group III, Lesions seen in HIV infection
Candidiasis	Bacterial infections	Bacterial infections
Erythematous	*Mycobacterium avium intracellularae*	*Actinomyces Israeli*
Pseudomembraneous	*Mycobacterium tuberculosis*	*Escherichia coli*
		Klebsiella pneumonia
Hairy leukoplakia	Melanotic hyper pigmentation	Cat-scratch disease
Kaposi's sarcoma	Necrotizing (ulcerative) stomatitis	Drug reactions (ulcerative, erythema multiforme, lichenoid, toxic epidermolysis)
Non-Hodgkin's lymphoma	Salivary gland disease	Epithelioid (bacillary) angiomatosis
Periodontal disease	Dry mouth due to decreased salivary flow rate	Fungal infection other than candidiasis
Linear gingival erythema		*Cryptococcus neoformans*
Necrotizingulcerative gingivitis		*Geotrichum candidum*
Necrotizing ulcerative Periodontitis		*Histoplasma capsulatum*
		Mucoraceae (mucormycosis zygomycosis)
		Aspergillus flavus
	Unilateral or bilateral swelling of major salivary glands	Neurological disturbances
		Facial palsy
		Trigeminal neuralgia
	Thrombocytopenia purpura	Viral infections
		Cytomegalovirus
		Molluscum contagiosum
	Ulceration NOS (not otherwise specified)	
	Viral infections	
	Herpes simplex virus	
	Human papilloma virus (warty-like) lesions	
	Condyloma acuminatum	
	Focal epithelial hyperplasia	
	Verruca vulgaris	
	Varicella-zoster virus	
	Herpes zoster	
	Varicella	

Table 2. Consensus Classification of Orofacial Lesions Associated with Paediatric HIV Infection (Ramos-Gomez *et al*, 1999)

Group I, Lesions commonly associated with paediatric HIV infection.	Group II, Lesions less commonly associated with paediatric HIV infection.	Group III, Lesions strongly associated with HIV infection but rare in children.
• Candidiasis • Erythematous • Pseudomembraneous • Angular cheilitis	Bacterial infections of oral tissues	Neoplasms Kaposi's sarcoma non-Hodgkin's lymphoma
Herpes simplex virus infection	• Periodontal diseases • *Necrotizing (ulcerative) gingivitis* • *Necrotizing (ulcerative) periodontitis* • *Necrotizing (ulcerative) stomatitis*	Oral hairy leukoplakia
Linear gingival erythema	Seborrheic dermatitis	Tuberculosis related ulcers
Parotid enlargement	• Viral infections • *CytomegalovirusHuman papillomavirus* • *Molluscum contagiosum* • *Varicella-zoster virus* • *Herpes-zoster* • *Varicella*	
Recurrent aphthous ulcers • Minor • Major • Herpetiform	xerostomia	

- Lesions strongly associated with HIV infection,
- Lesions less commonly associated with HIV infection and
- Lesions seen in HIV infection (ECClearinghouse, 1993).

Oral candidiasis

Oral candidiasis (OC) is the most frequent opportunistic fungal infection among human immunodeficiency virus (HIV)-infected patients with incident rate/density of 9.3 per 1000 person /months and a strong correlation with immune suppression as measured by reduced CD4 cell counts (<200 cells/mm^3) (Chattopadhyay *et al.,* 2005). It is the clinically visible oral manifestation of the disease.

In the early stages of HIV infection, candidiasis affects mainly the oral mucosa, the oesophageal mucosa being affected in more advanced stages of HIV disease (Kerdpon *et al.,* 2004). Oral candidiasis has been associated with a more frequent progression to AIDS, and it has been used as a clinical marker to define the severity of HIV infection (Kerdpon *et al.,* 2004). Candidal infection has been reported in adults with a prevalence varying from 1.5 to 56% with a higher prevalence in the developing world. *Candida albicans* is the predominant yeast colonizing the oral cavity of both healthy subjects and HIV-infected individuals in the developed as well as the developing world This yeast being isolated from 10 to 96% of HIVinfected subjects and 10–68% of healthy persons (Blignaut *et al.,* 2002). Other *Candida* species, such as *C. glabrata*, *C. krusei* and *C. tropicalis* are isolated more commonly from

HIV-infected persons (up to 30.7% of all yeasts) than immunocompetent individuals (15.9%) (Blignaut *et al.,* 2002). *Pseudomembraneous Candidiasis* [Fig 1, 2 and 3] is the most common clinical presentation (ranging from 55.8 to 69.7% of all candidal infections), followed by erythematous candidiasis (EC) (25.7–50%), angular cheilitis (13.7– 27.1%) and hyperplastic candidiasis (0–1.7%) Early studies suggested that EC may indicate a less severely compromised immune system than the presence of pseudo membranous candidiasis (PC), the latter occurring in more advanced stages (Schulten *et al.* 1989). More recent longitudinal studies, however, suggests that EC and pseudomembraneous candidiasis are of similar prognostic importance for the progression of HIV disease. However, the erythematous disease has been occasionally reported to be more prevalent than PC (Khongkunthian *et al.,* 2001).

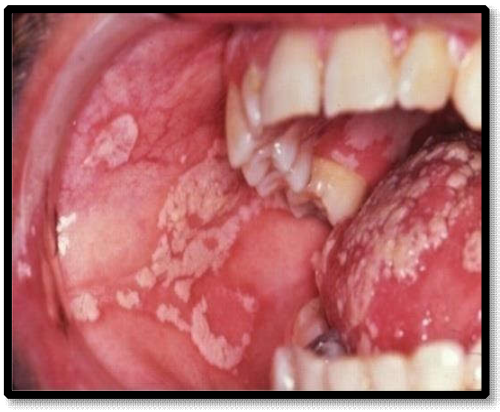

Figure 1:pseudomembraneous candidiasis on buccal mucosa and tongue

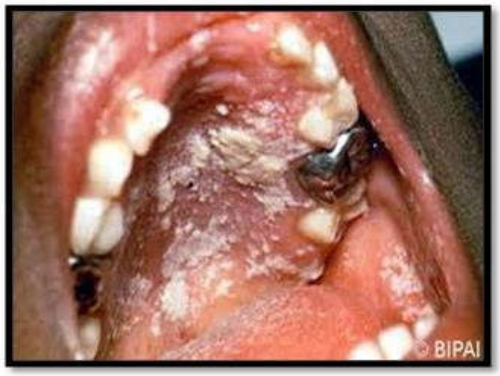

Figure 2. Pseudomembraneous candidiasis involving the palate

Figure 3. Angular chelitis

In *Pseudomembraneous type*, there will be white or yellow/creamy spots or plaques that may be located in any part of the oral cavity and can usually be wiped off to reveal an erythematous surface whereas in *erythematous type* there will be patchy erythema or red areas usually located on the palate and dorsum of the tongue, but occasionally on the buccal mucosa.

Treatment: Treatment is much difficult in patients with AIDS. Nystatin often is ineffective. Topical cotrimazole is associated with improved response and typically produces a clinical cure that equals that of the systemic azoles. But topical therapy is associated with a high recurrence rate. Systemic azoles (fluconazole, ketoconazole, itraconazole) produces longer disease-free in intervals but may cause drug resistant candidiasis (Magalhaes *et al.,* 2001). Itraconazole in an oral solution has been shown to be particularly effective in a swish and swallow method. Patients failing systemic azole therapy are candidiasis for intravenous amphotericin B if the patient's health supports its use.

Oral hairy leukoplakia

Oral candidiasis and OHL is predictive indicator for subsequent development of AIDS in HIV sero positive patients on the lateral margin of the tongue among young homosexual males. OHL is an EBV associated disease that typically occurs in the lateral border of the tongue of HIV infected individuals as a consequence of reactivation of the virus. The prevalence of OHL in recent studies of HIV-infected adults varies from 0.42 to 38%. In both the developed and developing countries OHL seems to be more common in males than females however a recent study observed the peak occurrence of OHL to be at 40–49 years in males, and 70 years in females. Clinically OHL appears as whitish/grey lesions on the lateral margins of the tongue.[figure 4 & 5] They are not removable and may exhibit vertical corrugations. Lesions range in size as they may be <1 cm, or may extend onto the ventral and dorsal surfaces of the tongue where they are usually flat. May be bilateral or unilateral. The lesion is somewhat distinctive (but not diagnostic) pattern of hyperkeratosis and epithelial hyperplasia that is characterised by white mucosal lesions that do not rub off (Fichtenbaum *et al.,* 2000; Fichtenbaum *et al,* 2003; Portela *et al.,* 2004).

HIV associated gingival and periodontal disease

The gingival and periodontal disease associated with HIV include linear gingival erythema, Necrotizing Ulcerative Gingivitis (NUG), periodontitis(NUP) and necrotising stomatitis (Walling *et al.,* 2003). Reported prevalence of HIV related gingival and periodontal disease (excluding opportunistic infection and malignancy) vary from 020% in children, while NUG and NUP are less prevalent varying from 2.2-5%.

LINEAR GINGIVAL ERYTHEMA is an unusual pattern of gingivitis that appears with a distinctive linear band of erythema that involves a free gingival margin and extends 2-3mm apically. In addition, the alveolar mucosa and gingival may demonstrate punctuate or diffuse erythema in a significant percentage of the cases. This form of gingivitis typically does not respond to improved plaque control and often exhibit a greater degree of erythema than would be expected for the amount of plaque in the area. In many instances, linear gingival erythema resolves after professional plaque removal, improved oral hygiene and use of chlorhexidine rinses. Cases resistant to initial therapy typically respond to systemic antifungal medications such as fluconazole or ketoconazole.

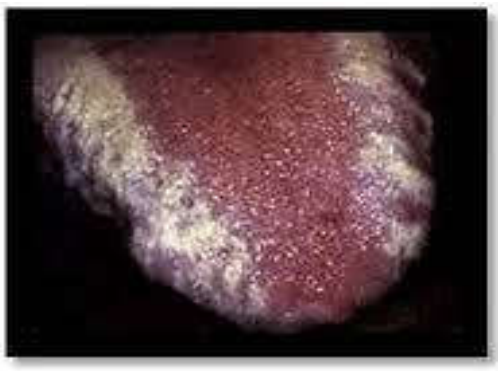

Figure 4. Oral hairy leukoplakia

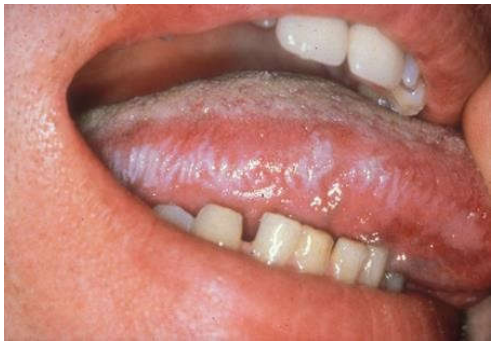

Figure 5.Oralhairyleukoplakia

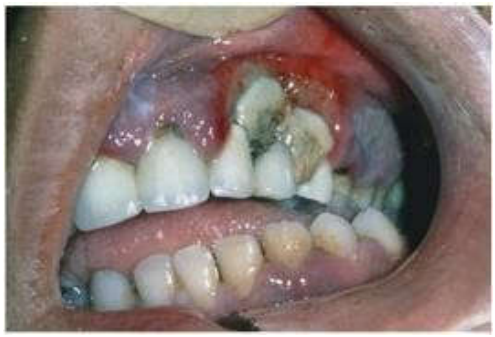

Figure 6. Necrotizing ulcerative gingivitis (www.google image.com)

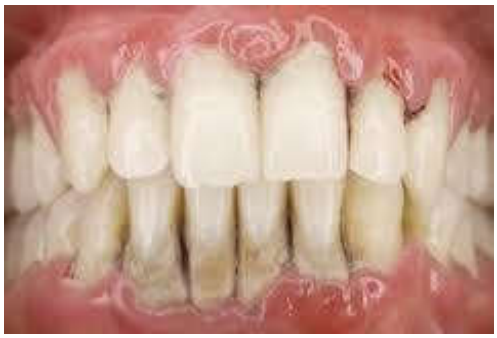

Figure 7. Necrotising ulcerative periodontitics (www.google image.com)

NUG refers to the destruction of one or more interdental gingival papillae. In acute stage of the process ulceration, necrosis and sloughing may be seen with ready haemorrhage and characteristic fetid odour [Figure:6]. In the case of **NECROTIZING ULCERATIVE PERIODONTITIS**, the condition is characterized by soft tissue loss as a result of ulceration or necrosis with exposure, destruction or sequestration of alveolar bone. The teeth may become loosened (Figure 7). The treatment of NUG and NUP revolves around debridement, antimicrobial therapy, immediate follow up care and long term maintenance. The initial removal of necrotic tissue is necessary, combined with povidone iodine irrigation. Systemic antibiotic is not necessary but metronidazole has been administered to patient with extensive involvement that is associated with severe acute pain. All patients should use chlorhexidine mouth rinses initially and for long term maintenance.

Kaposi's sarcoma

Kaposi sarcoma (KS) is a low grade neoplasm of endothelial origin that predominantly affects mucocutaneous sites, but may involve lymph nodes and internal organs (Raquel Dos Santos Pinheiro *et al.,* 2009). HHV8 is a gamma herpes virus that is an essential factor in the pathogenesis of KS, but by itself cannot cause KS (Pantanowitz *et al.,* 2010; Frezzini *et al.,* 2005; Antman *et al.,* 2000). Compared to other KS variants, AIDS-KS is a more aggressive disease typically with disseminated lesions and visceral involvement (Antman *et al.,* 2000). KS lesions in the mouth may be indolent or rapidly progressive & fulminent (Feller *et al.,* 2008). Oral KS may be unifocal or multifocal. A lesion may start as a single macule or as several macules that enlarge and coalesce. These more frequently may progress to papules, nodules or ultimately to exophytic masses that may become ulcerated (Petit *et al.,* 1986). Lesions range in colour from pink to bluish purple to deep brown and may vary in size from a few millimetres to several centimetres.

KS most frequently affects the palate, then the gingiva and tongue, rarely affects the floor of the mouth or ventro-lateral surface of the tongue (Pak *et al.,* 2007). Early oral KS lesions are usually asymptomatic, but advanced lesions may be painful, may become secondarily infected, may cause disfiguration, may interfere with speech and mastication or may even cause dysphagia (Feller *et al.,* 2008). Pain depends upon whether the lesions are ulcerated, are traumatised by opposing teeth or are secondarily infected (Lager *et al,* 2003). Long standing aggressive gingival KS may infrequently cause resorption of underlying alveolar process causing tooth mobility and even tooth loss (Kalpidis *et al.,*), as a result of direct pressure from KS or from the release of biological mediators (Figure 8, 9). A definitive diagnosis of oral KS is made by biopsy as KS may be clinically confused with bacillary angiomatosis, haemangioma, pyogenic granuloma, inflammatory gingival enlargement, drug-induced gingival hyperplasia and certain malignancies (eg: melanoma, lymphoma,leukemia) (Antman and Chang 2000). A variety of modalities may be available for the treatment of oral AIDS-KS: local therapy (surgical excision, intralesional chemotherapy, intralesional sclerosing agents and photodynamic therapy) and systemic therapy (HAART, chemotherapy). Local treatment is the first choice for all epidemiological forms of oral KS except for AIDS- KS because local treatment has fewer side effects and complications than systemic therapy (Lausten *et al.,* 2003; Reichart *et al.,* 2003; Krown *et al.,* 1989; Bergfeld *et al.,* 1987).

Non Hodgkins lymphoma

Since 1985 aggressive B cell lymphoma has been classified as an AIDS defining illness and is the second most common causes associated with HIV. Present as a firm elastic, often somewhat reddish swelling, with or without ulceration.

Figure 8. Multifocal oral AIDS-Kaposi sarcoma (KS) lesions on the buccal gingival

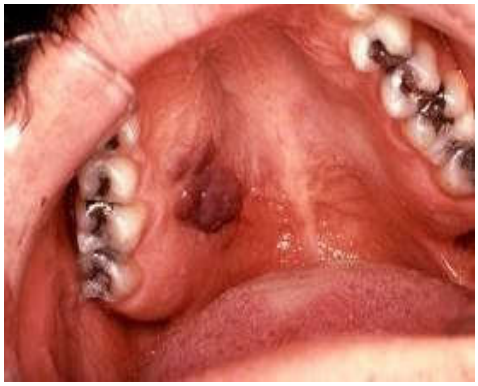

Figure 9. Kaposi's sarcoma affecting the palate

The gingiva, palatal mucosa, and fauces are sites of predilection. Biopsy, supported by appropriate treatment includes combination of chemotherapy and radiation (Fichtenbaum *et al.,* 2000).

Oral lesions as indicators of HIV infection

The main factor associated with the development of oral lesions and especially oral candidiasis is the CD4 count (Di Lorenzo *et al.,* 2007). The onset of oral candidiasis and OHL is heralded by a sustained reduction in the CD4+ blood cell count associated with sharp increases in viral load (Aboulafia, 2010). Disease progression is characterised by an increased prevalence of oral candidiasis, oral hairy leukoplakia, ulcerative periodontal disease and xerostomia (Margiotta *et al.,* 1999). An oral health care professional diagnosing these lesion in a patient known to be infected with HIV should be at least to the possibility of disease progression (Ramirez-Amador *et al.,* 2003). The interaction between CD4 counts and viral load prior to the development of oral candidiasis and oral hairy leukoplakia emphasis the potential use of oral lesion as early clinical indicators of HIV progression (Aboulafia *et al.,* 2010).

Role of healthcare professional in prevalence of oral manifestation

A consensus meeting of experts of the American Dental Association held in Chicago USA in 1992 stated that it was both safe and desirable to make regular dental care available to HIV patients (Greenspan, 1997). No modification of treatment is recommended except when patient have low CD4+ lymphocyte levels that predispose to oral lesion requiring specific treatment. if they have reduced platelet count below 60000 cells/mm^3 this may affect clotting time and patients with reduced neutrophil level below 500 cells/mm^3 may require antibiotic prophylaxis. Patient with late stage AIDS may require a rolling treatment plan (ie; frequent treatment evaluation) with regular reviews. An overall treatment strategy based on the treatment of symptoms or the provision of antiretrovirals, should include the management of oral conditions associated with HIV infection. Enhanced care comprised bimonthly protective treatment and chlorhexidine mouth rinses to treat gingivitis improves oral health. This improvement is associated with an improvement in both physical and mental health, but has no detectable effect on AIDS related complications, symptoms or mortality. Clinicians are advised to optimize oral hygiene, establish regular review periods, screen for HIV-related oral lesions and treat them if necessary and to screen for xerostomia as a possible symptom of HIV or as a side-effect of HAART.

Conclusion

Oral manifestations of HIV infection represent an important issue in the AIDS epidemic. Many HIVinfected individuals suffer from any HIV-related oral lesions (HIV-OL) during the course of the disease, with the corresponding impact on their quality of life. These lesions are readily accessible and can be diagnosed, with high degree of reliability, from the clinical features alone. HIV related oral lesion have been shown to be first sign of HIV infection in both industrialized (oral candidiasis, oral hairy leukoplakia) and resource poor countries (oral candidiasis, herpes zoster, noma). Oral examination by healthcare workers of all individuals at risk of infection or diagnosed HIV infected is mandatory. We must encourage research studies that investigate the prognostic value of Oro facial manifestations and oral health status as indicators of progression of HIV disease.

REFERENCES

Aboulafia DM. 2010. Evaluation and management of patients with Kaposi sarcoma. In: Pantanowitz L, Stebbing J, Dezube BJ, eds. Kaposi sarcoma. A model of oncogenesis. Kerala, India: Research Signpost, 339–60.

Antman K, Chang Y. 2000. Kaposi's sarcoma. *N Engl J Med.,* 342: 1027–38.

Barasch A, Safford MM, Catalanotto FA, Fine DH, Katz RV. 2000. Oral soft tissue manifestations in HIVpositive vs. HIV-negative children from an inner city population: a two-year observational study. *Pediatr Dent.,* 22: 215–20.

Beena VT, Kanaram Choudhary, R Rajeev, R Sivakumar, R Heera, S K Padmakumar, 2013. Review Article "human immunodeficiency virus vaccine an update" *Journal of Oral and Manifestation Pathology,* Volume 17 issue 1 Jan – 76.

Bergfeld WF, Zemtsov A, Lang RS. 1987. Differentiation between AIDS-related and non-AIDS-related Kaposi's sarcoma. *Cleve Clin J Med.,* 54: 315–9.

Blignaut E, Messer S, Hollis RJ, Pfaller MA. 2002. Antifungal susceptibility of South African oral yeast isolates from HIV/AIDS patients and healthy individuals. *Diagn Microbiol Infect Dis.,* 44: 169–74.

Burket's Oral Medicine – eleventh edition, Greenberg, Glick ship; 502

Chattopadhyay A, Caplan DJ, Slade GD, Shugars DC, Tien HC, Patton LL. 2005. Incidence of oral candidiasis and oral hairy leukoplakia in HIVinfected adults in North

Carolina. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.,* 99: 39– 47.

Di Lorenzo G, Konstantinopoulos PA, Pantanowitz L, Di Trolio R, De Placido S, Dezube BJ. 2007. Managementof AIDS-relatedKaposi's sarcoma. *Lancet Oncol.,* 8: 167–76.

Feigal DW, Katz MH, Greenspan D, et al. 1991. The prevalence of oral lesions in HIV-infected homosexual and bisexual men: three San Francisco epidemiological cohorts. AIDS, 5: 519–25.

Feller L, Anagnostopoulos C, Wood NH, Bouckaert M, Raubenheimer EJ, Lemmer J. 2008. Human immunodeficiency virus-associated Kaposi sarcoma as an immune reconstitution inflammatory syndrome: a literature review and case report. *J Periodontol.,* 79: 362–8.

Fichtenbaum CJ, Zackin R, Rajicic N, Powderly WG, Wheat LJ, Zingman BS. 2000. Amphotericin B oral suspension for fluconazole-refractory oral candidiasis in persons with HIV infection. Adult AIDS Clinical Trials Group Study Team 295. *AIDS*, 14: 845–52.

Frezzini C, Leao JC, Porter S. 2005. Current trends of HIV disease of the mouth. *J Oral Pathol Med.,* 34: 513–31.

Gottlieb MS, Schoroff, Schanker H M, Weisman J D, Fan PT, Wolf RA et al, 1981. Pneumo Cystitis carini pneumonia and mucosal candidiasis in previously healthy homosexual men evidence of a new acquired cellular immunodeficiency. *N.Engl J Med.,* 305;1425-31

Greeanspan JS. 1997. Sentinels and signports the epidemiology and significance of the oral manifestation of HIV diseases, 3 Suppl 1:s 13-17

Greenspan D, Canchola A, MacPhail L, Cheike B, Greenspan J. 2001. Effect of highly active antiretroviral therapy on frequency of oral warts. *Lancet*, 357: 1411–2.

Greenspan JS, Greenspan D. 2002. The epidemiology of the oral lesions of HIV infection in the developed world. *Oral Diseases,* 8 suppl2:34-9

Greenspan JS. 1997. Sentinels and signposts: the edipemology and significance of the oral manifestations of HIV diseases. *Oral diseases,* 3 suppl., 1:S13-17.

Kalpidis CD, Lysitsa SN, Lombardi T, Kolokotronis AE, Antoniades DZ, Samson J. 2006. Gingival involvement in a case series of patients with acquired immunodeficiency syndromerelated Kaposi sarcoma. *J Periodontol.,* 77: 523–33.

Kerdpon D, Pongsiriwet S, Pangsomboon K, et al. 2004. Oral manifestations of HIV infection in relation to clinical and CD4 immunological status in northern and southern Thai patients. *Oral Dis.,* 10: 138–44.

Khongkunthian P, Grote M, Isaratanan W, Piyaworawong S, Reichart PA. 2001. Oral manifestations in 45 HIV-positive children from Northern Thailand. *J Oral Pathol Med.,* 30: 549–52.

Krown SE, Metroka C, Wernz JC. 1989. Kaposi's sarcoma in the acquired immune deficiency syndrome: a proposal for uniform evaluation, response, and staging criteria. AIDS Clinical Trials Group Oncology Committee. *J Clin Oncol.,* 7: 1201–7.

Lager I, Altini M, Coleman H, Ali H. 2003. Oral Kaposi's sarcoma: a clinicopathological study from South Africa. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.,* 96: 710.

Lausten LL, Ferguson BL, Barker BF, Cobb CM. 2003. Oral Kaposi sarcoma associated with severe alveolar bone loss: case report and review of the literature. *J Periodontol.,*74: 1668–75.

Magalhaes MG, Bueno DF, Serra E, Goncalves R. 2001. Oral manifestations of HIV positive children. *J Clin Pediatr Dent.,* 25: 103–6.

Margiotta V, Campisi G, Manucuso S,Accurso V, Abbadessa V. 1999. HIV infection: oral lesion, CD4+ cell count and viral load in an Italian study population. *Journal of oral pathology and medicine,* 28:173-7.

Pak F, Mwakigonja AR, Kokhaei P, et al. 2007. Kaposi's sarcoma herpesvirus load in biopsies of cutaneous and oral Kaposi's sarcoma lesions. *Eur J Cancer.,* 43: 1877.

Palmer GD, Robinson PG, Chalacombe SI, Bimbaum W, Croser D, Erridge PL et al. 1996. Aetiological factors for oral manifestation of HIV infection. *Oral diseases,* 2:193-7.

Pantanowitz L, Stebbing J, Dezube BJ. 2010. Overview of Kaposi sarcoma. In: Pantanowitz L, Stebbing J, Dezube BJ, eds. Kaposi sarcoma. A model of oncogenesis. Kerala, India: Research Signpost, 1–40.

Patton LL, JA Phelan, FJ Ramos-Gomez, W Nittayananta, CH Shiboski, TL Mbuguye, 2002. "Prevalence and classification of HIV associated oral lesions" *Oral Diseases,* Volume pages 98–109.

Patton LL, McKaig RG, Eron JJ Jr, Lawrence HP, Strauss RP. 1999. Oral hairy leukoplakia and oral candidiasis as predictors of HIV viral load. *AIDS*, 13: 2174–6.

Patton LL, V Ramirez- Amador, G Anaya Saavedra, W Nittyananta, M Carrozzo, K Ranganathan, 2013. Oral Myth series." Urban legends series : oral manifestations of HIV infection." *Oral diseases,* 19, 533-550.

Petit JC, Ripamonti U, Hille J. 1986. Progressive changes of Kaposi's sarcoma of the gingiva and palate. Case report in an AIDS patient. *J Periodontol.,* 57: 159–63.

Portela MB, Souza IP, Costa EM, Hagler AN, Soares RM, Santos AL. 2004. Differential recovery of Candida species from subgingival sites in human immunodeficiency virus-positive and healthy children from Rio de Janeiro, *Brazil. J Clin Microbiol.,* 42: 5925–7.

Ramirez-Amador V, Esquivel-Pedraza L, SierraMadero J, Anaya-Saavedra G, Gonzalez-Ramirez I, Ponce-de-Leon S. 2003. The changing clinical spectrum of human immunodeficiency virus (HIV)-related oral lesions in 1,000 consecutive patients: a 12-year study in a referral center in Mexico. Medicine (Baltimore), 82: 39–50.

Ramirez-Amador V, Esquuivel-Pedraza L, SierraMadero J,Anaya-Saavedra G, Gonazalez-Ramirez I, Ponce –de-Leon S. 2003. The changing clinical spectrum of human immunodeficiency virus (HIV)-related oral lesions in 1,000 consequtive patients. A twelve – year study in a referral center in Mexico. medicine., 82:39-50.

Raquel Dos Santos Pinheiro,Talita Tenório França,Camila Maria Beder Ribeiro,Jair Carneiro Leão, Ivete Pomarico Ribeiro De Souza[4], Gloria Fernanda Castro, 2009. "Oral manifestations in human immunodeficiency virus infected children in highly active antiretroviral therapy era" *Journal of Oral Pathology & Medicine,* Volume 38, Issue 8, pages 613–622.

Reichart PA, Khongkhunthian P, Bendick C. 2003. Oral manifestations in HIV-infected individuals from Thailand and Camobodia. *Med Microbiol Immunol.,* 192: 157–60.

Scheifele C, Reichart PA, Dietrich T. 2003. Low prevalence of oral leukoplakia in a representative sample of the US population. *Oral Oncol.,* 39: 619–25.

Schulten EA, ten Kate RW, van der Waal I. 1989., Oral manifestations of HIV infection in 75 Dutch patients. *J Oral Pathol Med.,* 18: 42–6.

Shafer's Textbook of oral pathology 6th edition

Walling DM, Flaitz CM, Nichols CM. 2003. Epstein-Barr virus replication in oral hairy leukoplakia: response, persistence, and resistance to treatment with valacyclovir. *J Infect Dis.,* 188: 883–90.

Textbook of oral and maxillofacial pathology ;Neville 1999 International Workshop for a Classification of Periodontal Diseases and Conditions. Papers. Oak Brook, Illinois, October 30-November 2, 1999. *Ann Periodontol.,* 1999; 4: 112.

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