

# HIV - A Dental Perspective

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## ABSTRACT

The treatment of patients infected with HIV (human immunodeficiency virus) is a very interesting discipline within both medicine and dentistry. Recent advances in antiretroviral therapies have resulted in infected patients now having much longer symptom-free life spans and treatment planning now challenges the clinician to be cognisant of all the oral and dental aspects of the disease and its treatment. As well as influencing the epidemiology of the classical HIV-related lesions and infections, these drugs are associated with many drug interactions and adverse side effects. This review aims to describe the significant oral manifestations of the disease and highlight difficulties in managing this subset of patients.

## INTRODUCTION

Since acquired immunodeficiency syndrome (AIDS) was first recognized in 1981, there has been a global pandemic with devastating consequences. Patients with AIDS were unlikely to survive more than a year or two and they had to live with the dreadful social stigma associated with the disease.<sup>1</sup> Since then, scientists have developed an effective arsenal of drugs against the causative agent, human immunodeficiency virus (HIV). Dr. David Ho introduced highly active antiretroviral therapy (HAART) in 1995<sup>2</sup> and it has transformed the infection from a death sentence to a chronic disease.<sup>3</sup> Systematic reviews have shown that HAART or "triple therapy" has undoubtedly been a huge success in halting AIDS progression and suppressing viral load, relative to anti-retroviral therapies only using one or two drugs.<sup>4,5</sup>

By the end of 2003 there had been 3,408 cases of HIV reported in Ireland with 399 new cases in 2003 alone.<sup>6</sup> Even though AIDS mortality rates have declined, it is worrying that from 1994 to 2003 the Irish annual incidence of newly diagnosed HIV infections per year has increased by almost five fold.<sup>6</sup> With HAART, patients who are HIV-positive are living longer and are therefore demanding more from the health services.

## CLINICAL ASPECTS

HIV-related oral conditions are numerous, usually prominent and occur early in the disease process. These potentially pathognomonic manifestations have been well classified.<sup>7,8,9,10</sup>

Many reports have focused on the changing spectrum of HIV-related oral lesions in the era of HAART. Oral candidiasis (OC), oral hairy leukoplakia (OHL), HIV-related periodontal

Stage of HIV/AIDS	Possible related oral lesion or infection
Acute seroconversion illness	Aphthous ulceration and oral candidiasis
HIV-infection in Undiagnosed individual	Oral candidiasis, oral hairy leukoplakia, Kaposi's sarcoma, necrotizing ulcerative gingivitis
Clinical disease progression/predictor of development of AIDS	Oral candidiasis and oral hairy leukoplakia
Immune suppression in HIV	Oral candidiasis, oral hairy leukoplakia, necrotizing periodontal disease, Kaposi's sarcoma, long-standing herpes infection and major aphthous ulcerations

**Table 1.** Possible oral lesions in relation to the clinical spectrum of HIV/AIDS.

disease and Kaposi's sarcoma (KS) have declined in prevalence by varying amounts in different parts of the world. Tappuni and Fleming found that oral manifestations of HIV were found in 30 percent of subjects taking any antiretroviral regimen compared to 46 percent for drug naïve HIV-positive patients.<sup>11</sup> Eyeson et al suggested that substantial differences in prevalence reported for different lesions might be due to inconsistencies between study groups, different study designs and inter-examiner variation.<sup>12</sup> It has been widely observed that oral lesions are associated with CD4+ T cells counts less than 200 /mm<sup>3</sup> and/or plasma HIV RNA greater than 3,000 copies/ml, whether the patient was taking antiretrovirals or not.<sup>11,13,14</sup>

Study (year)	OC (%)	OHL (%)	HIV-necrotizing periodontal disease (%)
Margiotta et al. (1999) <sup>15</sup>	9.6	9.6	2.9
Patton et al. (2000) <sup>16</sup>	16.7	11.4	1.7
Schmidt-Westhausen et al. (2000) <sup>13</sup>	0	0	1.6
Eyeson et al. (2002) <sup>14</sup>	4.9	9.9	9.9

**Table 2.** Prevalence of strongly associated HIV oral lesions in the era of HAART.

Candidiasis is often the initial manifestation of HIV.<sup>17,18</sup> The infection may present early in immune dysfunction in two main forms. Initially erythematous candidiasis (EC) presents at higher CD4+ T cell counts (approximately 400 cells/mm<sup>3</sup>), followed by pseudomembranous candidiasis (PC) that occurs more commonly when CD4+ T cell counts decrease to around 200 cells/mm<sup>3</sup>.<sup>7</sup> Both forms reportedly occurred in 8 percent of patients on HAART compared to 21 percent and 11 percent (for EC and PC respectively) in drug naïve patients.<sup>11</sup> Angular cheilitis and rarely hyperplastic candidiasis are also seen with HIV.<sup>19</sup> It has recently been demonstrated that protease inhibitors (PIs), which are common components in HAART regimens, may directly inhibit a family of candidal virulence enzymes, candida-secreted aspartyl proteinase (Sap). This may explain how the beneficial effect of PIs against OC is independent of the effects of early immune reconstitution.<sup>20</sup> It is interesting to note that a retrospective Spanish study found that HAART influenced a significant reduction in PC but with a compensatory increase in EC thus indicating a partial immune recovery in those affected.<sup>21</sup> Currently, a Cochrane Review is researching the methods of preventing and treating OC in HIV disease.<sup>22</sup> This study will compile the results of relevant, randomised controlled clinical trials and its outcome may be useful to clinicians treating this common infection. Problems encountered in the treatment of OC include the development of resistance and drug-drug interactions. It has been reported that up to 10 percent of candida isolates become azole resistant in HIV-infected individuals.<sup>23</sup> Also, there is a potential risk of reaching toxic plasma azole levels when these anti-fungal agents are co-administered with PIs. Therefore, great caution must be exercised when PIs and azole anti-fungals are used concomitantly; it should be noted that a parallel dilemma occurs with the use of the macrolide antibiotics.<sup>24,25,26,27</sup>

Herpes simplex and zoster infections occur commonly in HIV-disease and are routinely treated with aciclovir. However, both aciclovir and ganciclovir increase HAART toxicity and therefore the combination of these agents demands considerable caution.<sup>27</sup> This difficult issue is worsened by the fact that ganciclovir is the treatment of choice for cytomegalovirus infections which may be severe in HIV disease.

Destructive periodontal disease is a serious dental condition that often renders the patient edentulous

and it is widely associated with counts less than 200 CD4+ T cells/mm<sup>3</sup>. Necrotizing ulcerative gingivitis (NUG), an acute, severe infection of the gums, is one variant of this disease. In one study, the incidence of NUG was zero percent in those patients taking HAART, compared with six percent of the drug naïve HIV-positive cohort.<sup>11</sup> It is also worth noting that there is a greater incidence of dental caries in patients infected with HIV.<sup>28,29</sup>

OHL is virtually exclusive to HIV-positive patients with low immunocompetence. Therefore it is not surprising that it is now less common with successful antiretroviral therapy. Research has shown that adult smokers are approximately three times more likely than non-smokers to have periodontal disease<sup>30</sup> because tobacco-induced alterations in microbial and host factors have deleterious effects on the periodontium.<sup>14,31</sup> It is thus interesting to note that it has also been reported that smoking increases the prevalence of HIV-specific lesions, namely OHL and condylomata acuminata.<sup>13</sup>

KS has been described as a sinister, opportunistic neoplasm associated with advanced immunosuppression. The average survival of patients is 21 months (range three to 45 months). In 60 percent of cases of KS, there is oral involvement and this usually involves the hard palate.<sup>19</sup> Oral KS has a prevalence of zero to 38 percent in the HIV-infected population worldwide and is seen predominantly in populations where men have sex with men.<sup>10</sup> With this particular mode of transmission, the receiving partner is most at risk of HIV transmission and at a similar risk to infected needle sharers.<sup>32</sup> It is suggested that KS-associated human herpes virus 8 may be transmitted as a cofactor in these instances. With HAART, oral KS has declined up to four-fold<sup>13,33</sup> and is seen as the mainstay palliative treatment of this cancer.<sup>19</sup>

Conversely, the prevalence of HIV-related salivary gland disease and herpes-virus infections has increased with HAART and human papillomavirus (HPV)-associated oral warts are reported to have increased up to six-fold.<sup>13,16,34,35</sup> This increase is of concern because some HPV are linked with malignant disease, for instance HPV-16, 18 and 33 have been associated with cervical carcinoma.<sup>36</sup> With HAART, an incompletely reconstituted immune system may vary in functionality against pathogenic microorganisms due to the CD8+ T cell diffuse infiltrative syndrome that is part of

immune reconstitution syndrome, thus the increase of salivary gland disease is expected.<sup>32</sup> This phenomenon has been referred to as the “HAART attack” where recrudescence of latent disease occurs with renewed immune competence.

Antiretroviral therapy is strongly linked with xerostomia, which was reported in up to one-third of patients taking didanosine who had AIDS or AIDS-related complex and had previously demonstrated haematological intolerance to zidovudine.<sup>37</sup> In patients taking HAART, including PIs, up to seven percent have reported xerostomia and/or oral ulceration.<sup>38</sup> Patients taking HAART may also present complaining of facial numbness or tingling which may even have resulted in accidental traumatic injury. Circumoral paraesthesia was reported in 25 to 27 percent of patients on PIs<sup>36,39,40</sup> but in only two percent of patients interviewed by Schmidt-Westhausen *et al*,<sup>13</sup> who proposed that the large difference occurred because their patients did not report this symptom due to its short duration and spontaneous resolution. Taste abnormalities are also linked to the use of PIs<sup>1,25,39</sup> and research shows the prevalence of this adverse effect as being between 10 to 20 percent.<sup>36</sup>

### Cross Infection Management Issues

Dentists have a professional duty of care to treat HIV-positive patients without discrimination and HIV-serostatus should not impinge on treatment planning. Regular care is essential in managing HIV-related oral diseases and this treatment should be provided more slowly and carefully if necessary.<sup>41,42,43,44</sup> Asymptomatic patients taking HAART may not necessarily disclose their HIV-serostatus or medication regimen to the dental team and universal precautions should be observed at all times which are designed to safeguard both the patient and healthcare workers against cross-infection. The risk of seroconverting following a needlestick injury from an infected patient is approximately 1:300<sup>30,45</sup> and the availability of post exposure prophylaxis should not cause complacency in healthcare workers.

- The viral load of the carrier (HIV RNA <1,500 copies/ml considered low risk)
- Whether to patient is currently on a HAART regimen
- Dental needles are usually have a small bore unlike those used for venepuncture
- Needles may be “cleansed” by passing through a protective rubber glove
- Deep, penetrating wounds usually occur with scalpels in oral surgery or periodontal departments and not in general practice

**Table 3.** Factors that influence and potentially lower the risks in the dental setting.

Successful HAART results in increased numbers of B lymphocytes, T lymphocytes, polymorphonuclear leukocytes (PMNL) and platelets. However antiretroviral therapy does not dictate whether antibiotic prophylaxis is required. In general, it is not required for routine dental procedures in HIV-infection unless indicated by the patient’s medical history. Patients infected with HIV via intravenous drug use are reported to be at increased risk of developing infective endocarditis.<sup>44,46</sup> Apart from the massive transmission risk posed by HIV-infected blood transfusions, this group has the highest “per act risk of acquiring HIV”,<sup>30</sup> therefore it logically follows that infected needle sharers have a high risk of being co-infected with other pathogens at every exposure. Table 4 summarises a recent report on the topic in relation to HIV-infection.<sup>44</sup>

- Thorough review of patient’s history when count of <200 CD4<sup>+</sup> T cells/mm<sup>3</sup>
- Antibiotic cover recommended for oral and periodontal surgery if PMNL counts <500 cells/mm<sup>3</sup>
- Neutropenia
- Current guidelines should be adhered to in the country of treatment

**Table 4.** Protocol for use of antibiotic prophylaxis.

The use of antibacterial mouthrinse and scaling has been advocated prior to dental and surgical procedures. No scientific evidence exists to suggest an increased risk of post-operative local infection in HIV-positive patients. When it does occur, systemic oral antibiotics may be prescribed, taking into account the antiretroviral therapy the patient may be receiving. However the condition of the immune system in HIV disease may alter symptoms of infection, such as reduced inflammation or lack of purulence in patients with lower immune competence.<sup>44</sup>

### CONCLUSIONS

HIV-disease and its treatment is an ever-evolving discipline within medicine. It behoves the dental practitioner to be familiar with the current treatment methods for this expanding subset of patients and the challenges that they bring. Regular oral examination may alert the clinician to a change in the status of HIV-infection and therefore prompt appropriate care, whether it is the curative treatment of opportunistic infections or palliative care in the later stages of the disease. Candidiasis is still seen all too frequently in these patients and its management may not necessarily be as straightforward as it is in HIV-negative patients. HIV-related periodontal disease, Kaposi’s sarcoma and oral hairy leukoplakia are

orally-manifesting conditions that can be readily flagged by the attending dentist.

Side effects of HAART regimens will exercise the practitioner, whether it is to reassure patients who develop erythema multiforme or to alert the supervising specialist about more hazardous adverse reactions. HAART-related xerostomia and its inherent problems often require dental intervention and expertise. Drug interactions are particularly important as antiretroviral agents may interfere with relatively commonly prescribed drugs such as metronidazole and antifungal agents

and may cause life-threatening respiratory depression when combined with common sedative agents.

It should be noted that HIV-infected CD4+ T cells have been found in follicular dendritic and lymph node mononuclear cells in patients who had undetectable plasma viraemia.<sup>47</sup> This highlights the fact there is no cure for HIV-disease and also reminds the healthcare worker about the serious nature of the infection, even if it is well masked by successful antiretroviral therapies.

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