Dentists and HIV

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This resource is written for dentists to provide an overview of the oral manifestations and complications associated with HIV infection and treatments. The responsibilities of dentists when managing a suspected HIV-associated oral condition in a patient with known, or unknown status, is also discussed.

The burden of HIV infection

By the end of December 2008, more than 28 000 diagnoses of human immunodeficiency virus (HIV) infection and more than 10 000 diagnoses of acquired immunodeficiency syndrome (AIDS) had been made in Australia, with some 7000 people having died from advanced HIV disease or AIDS.

There are now more than 17 000 people with HIV infection in Australia, with approximately 1000 people newly infected each year.[1] The life expectancy of people with HIV infection is increasing as improved antiretroviral treatments mean people are able to live longer, often for decades following HIV infection.[2] In fact, the definition of AIDS was largely based on the understanding that HIV was degenerative, with infection following a linear progression to the point that a person was seriously incapacitated, with little or no possibility for improvement. That is no longer the case, with numerous people having experienced an AIDS-defining illness at some time, but now at a less severe stage of disease progression. In 2008, 24 people in Australia died following an AIDS diagnosis.

HIV virology

HIV belongs to the retrovirus family. It contains two copies of single-stranded ribonucleic acid (RNA). The viral RNA is surrounded by a capsid made from viral proteins and this is enclosed in a viral envelope formed from the cellular membrane of the host cell.[3]

Following infection of a cell, viral RNA is converted to deoxyribonucleic acid (DNA). The viral DNA directs the transcription of viral RNA, which is directly incorporated into new viral particles or transcribed into viral proteins and subsequently integrated into newly formed virions.[4]

The main targets for HIV infection are cells in the immune system, particularly CD4 cells, which are a helper T-cell, carrying the CD4 surface antigen. CD4 cells are regulators and effectors of the normal immune response. Over time, CD4 cell counts decline, which results in a poorly functioning immune system (immunodeficiency). This eventually leads to AIDS, which is indicated by the diagnosis of one or more AIDS-defining conditions including opportunistic infections, malignancy, wasting and neurological disorders.

HIV transmission

HIV is transmitted from a person with the virus to a person without infection by exposure to HIV-infected bodily fluids or tissues. Internationally recognised modes of transmission include unprotected sex, re-using drug-injecting equipment, and vertical transmission from mother-to-child.[5,6] In Australia in 2008, among cases of newly acquired HIV infection, male homosexual contact was reported in 86% of cases, heterosexual contact in 10% of cases, and injecting drug use in 1% of cases (with undetermined exposure in 3%).[1] Cases of mother-to-child transmission are uncommon in Australia, as is transmission via needlestick injuries, tattooing and medical procedures.[5]

There is a 0.3% risk of HIV transmission after percutaneous exposure to HIV-infected blood.[7] HIV is present in saliva, however it is not considered a risk factor for transmission because of the low levels of HIV that can be detected, and the endogenous antiviral factors present in saliva.[8-10] There is no evidence that HIV can be transmitted by contact with tears, sweat, urine or faeces.[5,6]

The natural history of HIV infection

During the initial phase of infection there is a window period of several weeks or months, during which antibodies to HIV are not detectable. In this period many people develop mononucleosis or flu-like symptoms 2 to 6 weeks after acquiring the initial infection, a result of the host's systemic reaction to the virus and the mounting of an immune response. This brief illness, often referred to as a seroconversion illness, may last from days to weeks. Symptoms are variable but may include fever, malaise, headache, arthralgia, rash, tender lymph nodes, diarrhoea and oral manifestations and the number of CD4 cells may drop significantly. During this period, detectable antibodies to HIV and HIV-specific cytotoxic T-cells appear in serum. The peak viral load (VL) during the HIV seroconversion illness corresponds to the severity of the illness.[11] The resolution of the acute HIV seroconversion illness occurs when the host develops an immune response to the infection, although the individual never successfully clears the virus. After seroconversion, and the associated illness, CD4 cell counts rise again and HIV VL falls, however CD4 cell counts usually never return to pre-infection numbers.[12]

A clinical, asymptomatic phase then follows, which may last for 2 to 10 or more years. During this period there is a gradual fall in CD4 cells and a slow decline in immune function. As the CD4 cell count drops to below 500 cells/μL of blood (the lower limit of normal), the person may experience some symptoms, such as weight loss or increasing infections. Over time the CD4 cell count will decline further, to below 200 cells/μL. At this point more serious complications are likely to manifest with the occurrence of opportunistic infections or malignancies. This stage continues to be referred to as advanced HIV disease or AIDS.

Monitoring of HIV infection therefore involves routine checks of CD4 cell counts and VL. HIV VL is defined as the amount of HIV virus in the blood reported as the number of copies of HIV RNA in one millilitre (mL) of blood. The amount of circulating virus reflects the activity of the virus and will generally correlate with the degree of damage that is occurring to the immune system. A VL of greater than 100 000 copies/mL of blood is considered high.

Oral pathophysiology of HIV infection

As the immunodeficient state gradually impairs humoral and cell-mediated immunity it allows other diseases to affect the patient. New pathogens can more easily cause disease and often any disease will be more severe and widespread. Further, pre-existing conditions that remained latent or under the control of a functioning immune system can become re-activated and cause disease, as will normally non-pathogenic organisms, which may gain the ability to cause disease in the patient. These pathologies are defined as opportunistic infections.

Oral lesions may be present at all stages of HIV infection. However, it should be emphasised that HIV-associated oral lesions are not pathognomonic, as it is possible to find the conditions in immunocompetent people without HIV infection.[13] Similar to systemic HIV-associated pathology, the oral lesions presenting during HIV infection are more likely to occur with a high VL or a reduced CD4 cell count.[14-21] Oral manifestations of the seroconversion illness may include oral ulcers, oral candidiasis, oral herpes and tonsillitis and uncommonly gingivitis and stomatitis.[12,22] The failure of normal immune surveillance throughout the course of HIV infection also increases the risk of neoplasia. Neurological conditions associated with HIV infection and treatment may also be evident.

Treatment of HIV infection

The aim of treatment is to suppress HIV infection and to allow immune recovery. Ultimately this will prevent or lessen the likelihood of HIV-related complications, prevent AIDS and maintain health. Presently, treatment is very successful for most people with HIV infection, with current life expectancy from diagnosis projected to be almost 40 years for a young person.[23]

Treatment of HIV infection involves the use of combinations of antiretroviral drugs, currently referred to as combination antiretroviral therapy (cART). This treatment is instituted based on the monitoring of disease progression. Current guidelines recommend starting treatment when the CD4 cell count declines to 350 cells/μL.[24] The aim of treatment is to produce an undetectable VL of less than 50 copies/mL of HIV, measured by RNA polymerase chain reaction (PCR). Treatment may result in an increased CD4 cell count and reduced immunosuppression potentially resulting in the prevention or reversal of HIV-associated complications.[25]

Impact of HIV treatment on oral conditions

Oral manifestations may occur with the progression of HIV infection in patients without medical treatment or intervention. However, in Australia, most people with HIV infection will start a treatment regimen prior to significant immune impairment. The impact of cART generally results in a marked reduction in viral load, which in turn enables the immune system to return to adequate surveillance of the oral environment with oral manifestations often vanishing. Occasionally, some conditions such as aphthous ulceration may persist while HIV-related periodontal diseases may recur, even in the presence of adequate viral control. However, co-factors such as stress and smoking have been suggested to have a role in their re-emergence.[26]

Although introduction of cART often improves oral health and stabilises or cures existing oral conditions, some oral complications may result from the introduction of therapy. Generally, there appear to be few significant oral side effects associated with any particular medication. However, the combination of potent antiretroviral drugs with other medications may commonly result in xerostomia and dry lips. Often persistent cracking will occur at the anterior commissure, which appears to have no causative fungal or obvious pathogen involvement. The dryness of the mouth can often cause rapid dental decay, which is particularly significant if pre-existing HIV-related periodontal diseases have caused significant damage to root structure.

Oral conditions associated with HIV infection and the development of advanced HIV disease can be aetiologically divided into five major groups:[27]

- Microbiological infections (fungal, bacterial, viral)
- Oral neoplasias
- Neurological conditions
- Lesions of uncertain aetiology
- Oral conditions associated with HIV treatment.

Other co-infections and conditions associated with HIV infection, which are significant to dentists are:

- Syphilis
- Tuberculosis
- Persistent generalised lymphadenopathy
- Gastro-oesophageal reflux disease (GORD)
- Odynophagia.

Microbiological infections

Fungal Infections

Mycoses or fungal infections are often the first and most prevalent conditions affecting the oral mucosal surfaces of patients with HIV infection.[13,15,21,28,29] The main fungal pathogen involved in oral disease is *Candida albicans*, however numerous other fungi have been reported as pathogens.[13] The unusual or systemic mycoses can have oral manifestations, however these will not be covered within this document. The classic forms of oral candidiasis described below include erythematous candidiasis, pseudomembranous candidiasis, angular cheilitis and chronic hyperplastic candidiasis. Linear gingival erythema is now classed as a periodontal condition of fungal origin.[30]

Fungal infections may appear at any time throughout HIV infection, however they are more prevalent when the CD4 cell count falls to below 500 cells/μL.[14,16,20,21] Ninety percent of patients with AIDS are affected with oral candidiasis at some point during their disease.[28] However cART results in a significant reduction of oral candidiasis, such that rates range from 0–16.7%.[20,21] Interestingly, cART has changed the patterns of prevalence of oral lesions associated with HIV infection, so now candidiasis is no longer the most common oral lesion.[20,21] Diagnosis of oral candidiasis is usually made on clinical grounds. Confirmation can be achieved by cytological smear using periodic acid Schiff stain or culture.

Erythematous candidiasis

- **Description:** patchy red or erythematous areas that may become diffuse and atrophic
- **Location:** commonly found on the hard palate and the dorsum of the tongue and occasionally on the buccal mucosa
- **Symptoms:** none or mild-to-moderate pain or burning
- **Duration:** usually intermittent, however may be chronic. The chronic form is often associated with dentures
- **Diagnosis:** clinical, with a swab for microscopy and culture when there is an uncertain diagnosis or poor response to treatment.

Figure 1: Erythematous candidiasis on the dorsum of the tongue

Pseudomembranous candidiasis

- **Description:** creamy white or yellow plaques which, when scraped, reveal an erythematous or bleeding mucosal surface
- **Location:** may be found on any of the intra-oral surfaces
- **Symptoms:** none or mild-to-moderate pain or burning
- **Duration:** usually intermittent, however may be chronic
- **Diagnosis:** clinical, with a swab for microscopy and culture when the diagnosis is uncertain or there is a lack of response to treatment.

Figure 2: Pseudomembranous candidiasis affecting palate, tongue and buccal mucosa

Angular cheilitis

Angular cheilitis is commonly associated with a concurrent infection with *Staphylococcus aureus*.

- **Description:** erythema and red or white fissures or ulcers at the corners of the mouth
- **Location:** found at the labial commissures
- **Symptoms:** none or mild-to-moderate pain or burning
- **Duration:** usually intermittent but can be chronic
- **Diagnosis:** clinical. Rarely however, taking a swab for microscopy and culture may be appropriate if there is an uncertain diagnosis or the lesion does not respond well to therapy.

Figure 3: Angular cheilitis affecting the corner of the mouth

Chronic hyperplastic candidiasis

This condition has an association with smoking. It is generally considered premalignant and the lesion may demonstrate dysplasia.[31]

- **Description:** speckled or homogenous white patches that are rough and irregular and cannot be wiped off. Clinically indistinguishable from leukoplakia and can be confused with oral hairy leukoplakia
- **Location:** most commonly found on the buccal mucosa near the labial commissures with less frequent involvement of the palate or tongue
- **Symptoms:** usually symptomless but speckled lesions may produce discomfort
- **Duration:** chronic
- **Diagnosis:** clinical, with a swab for microscopy and culture when there is an uncertain diagnosis or poor response to treatment.

Figure 4: Hyperplastic candidiasis of the palate

Figure 5: Hyperplastic candidiasis of the tongue

Linear gingival erythema

Linear gingival erythema is a gingival condition of immunosuppressed people. Growing evidence supports the theory of a fungal origin for this condition.[32,33] It is classified by the American Academy of Periodontology as a disease of fungal aetiology.[30] The lack of response of linear gingival erythema to oral hygiene measures and conventional periodontal therapy is important in diagnosis.[34]

- **Description:** initially discrete petechiae that may coalesce into a 1-3 mm wide, intensely erythematous band on the marginal gingivae. This condition is unlike gingivitis induced solely by dental plaque in that the erythema associated with linear gingival erythema is disproportionate to any local factors, such as plaque and calculus
- **Location:** found along the gingivae and may be localised or generalised
- **Symptoms:** usually no significant symptoms, however the gingival may be tender and bleed easily
- **Diagnosis:** clinical.

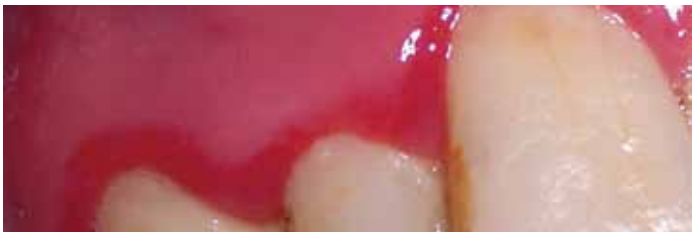

Figure 6: Linear gingival erythema

Treatment for oral fungal infections

Treatment with topical antifungals can be initiated by a dentist, however systemic antifungal therapy should be prescribed by the patient's general practitioner (GP). It is best practice to consult with a patient's GP before commencing any systemic medications.

Dental management of oral candidiasis

- Miconazole 2%: 2.5 mL of gel dropped on the tongue and kept in the mouth for as long as possible before swallowing. Should be taken after meals and for 14 to 21 days.[35]

OR

- Amphotericin B lozenges: one lozenge slowly dissolved in the mouth four to eight times a day for 14 to 21 days.[35]

Dental management of angular cheilitis

For angular cheilitis, treat oral candidiasis as above and in addition recommend:

- Miconazole 2% cream or gel topically, four times daily to the angles of the mouth for at least 14 days.[35]

OR

- Nystatin 100 000 units/g cream topically, two to three times daily to the angles of the mouth for at least 14 days.[35]

Consideration should be given to the risk of decay from nystatin liquid, as it is sweetened with sugar.

Dental management of linear gingival erythema

Refer to the *Treatment of HIV-associated periodontal infections* box below.

Vacuum-formed treatment trays may be fabricated to hold the antifungal medicament against the infected tissue. If an inadequate response to topical medication is seen after 2 weeks, increasing the frequency and/or the dose of medication may be necessary. For recalcitrant infections, referral to a GP is required for prescription of systemic antifungals such as ketoconazole, fluconazole or itraconazole.

Where fluconazole-resistant forms of candidiasis are present, e.g. *Candida glabrata* and *Candida krusie*, mouthwash with ketoconazole can prove effective.

Bacterial Infections

There is a wide range of bacterial pathogens that cause oral disease in patients with HIV infection. This section will deal with bacterial periodontal infections associated with HIV infection as well as syphilis and tuberculosis.

Periodontal Infections

For dentists, the most significant oral manifestation of HIV-associated bacterial infections is periodontal pathology. These pathologies fall into three groups: linear gingival erythema, necrotising periodontal diseases and accelerated progression of chronic periodontitis. Linear gingival erythema is primarily a fungal disease and is discussed above, however it is worth mentioning here as linear gingival erythema may represent a precursor condition to necrotising ulcerative periodontal diseases associated with HIV infection.[34,36] The necrotising diseases of the periodontium include necrotising ulcerative gingivitis, periodontitis and stomatitis. The prevalence of necrotising periodontal diseases associated with HIV infection has reduced with the introduction of modern antiretroviral therapy.[34] The reported rates vary from 0.6% to 11%.[20,21,37] Necrotising ulcerative gingivitis and periodontitis are classified together as related conditions.[30] Necrotising ulcerative gingivitis, periodontitis and stomatitis are believed to be related, however the exact relationship between the conditions has yet to be fully delineated.[28,34] Particularly spirochetes but usual periodonto-pathogens are believed to be important in the pathogenesis of necrotising ulcerative gingivitis and periodontitis.[38,39] The exact role of *Candida* species remains to be determined in ulcerative periodontal diseases associated with HIV infection.[34] HIV infection enhances progression of chronic periodontitis.[40,41] The periodontopathic bacteria, fungi such as *Candida* and viruses such as human herpesvirus (HHV) have been examined and are implicated in the pathogenesis of chronic periodontitis in people with HIV infection.[34]

Necrotising ulcerative gingivitis

Necrotising ulcerative gingivitis presents with pain, ulceration and gingival bleeding. The lesion does not involve the alveolar bone.[34]

- **Description:** the characteristic lesion is a punched out, ulcerated and erythematous interdental papilla covered by a greyish necrotic slough
- **Location:** gingival tissues particularly the interdental papillae
- **Symptoms:** moderate-to-severe pain, bleeding and fetor oris. Systemic features such as fever, malaise and lymphadenopathy may be present
- **Duration:** sudden onset and rapidly deteriorating
- **Diagnosis:** clinical.

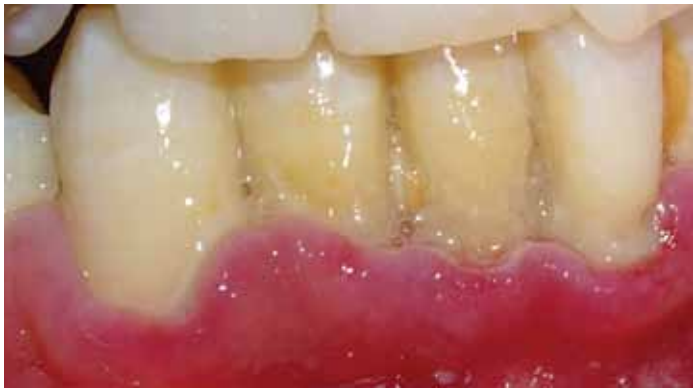

Figure 7: Necrotising ulcerative gingivitis

Necrotising ulcerative periodontitis

Necrotising ulcerative periodontitis presents identically to necrotising ulcerative gingivitis with pain, ulceration and gingival bleeding except the lesion involves the alveolar bone.[34]

- **Description:** ulcerated erythematous gingival tissues, particularly the interdental papilla, covered by a greyish necrotic slough. There may be exposed bone, gingival recession and tooth mobility
- **Location:** the interdental papilla extending into the deeper periodontal tissues
- **Symptoms:** moderate-to-severe pain, bleeding and fetor oris. Systemic features such as fever, malaise and lymphadenopathy may be present
- **Duration:** sudden onset and rapidly worsening
- **Diagnosis:** clinical.

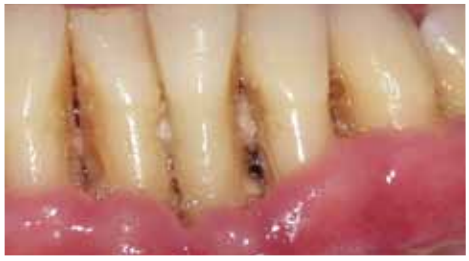

Figure 8: Necrotising ulcerative periodontitis

Necrotising ulcerative stomatitis

- **Description:** extensive area of ulceration, tissue necrosis and erythema that extends from gingival into the adjacent mucosa and may involve bone leading to osteonecrosis and sequestration
- **Location:** periodontal tissues and may extend into the maxillary or mandibular bone
- **Symptoms:** moderate-to-severe pain, bleeding, fetor oris. It is usually associated with systemic symptoms of fever, malaise and lymphadenopathy
- **Duration:** sudden onset and rapidly worsening
- **Diagnosis:** clinical.

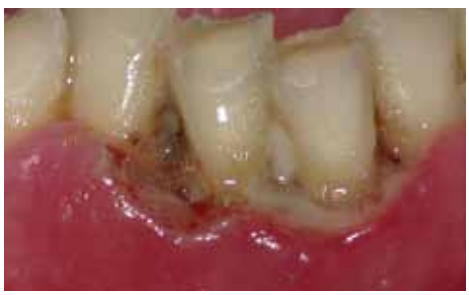

Figure 9: Necrotising ulcerative stomatitis

Treatment of HIV-associated periodontal infections

Currently there is inadequate information to provide dentists with evidence-based guidelines for the management of HIV-associated periodontal infections.[42,43] Periodontal diseases should be treated as they would be in people without HIV infection with removal of plaque, calculus and necrotic tissue.[34,42,44] Excellent home oral hygiene should be encouraged and smoking cessation recommended. Adjunctive therapies, such as irrigation and rinsing with 10% povidine iodine or 0.12%-0.2% chlorhexidine and the prescription of systemic antibiotics, should be considered on a case by case basis.[34,42,44] Narrow-spectrum antibiotics, such as metronidazole, are preferable to broad-spectrum antibiotics to reduce overgrowth of commensals and microorganism resistance.[34,44] The use of antifungals may be considered due to the implication of fungal disease in periodontal disease pathogenesis.[34] Consultation with the patient's GP is warranted before administration of systemic medication. The initial treatment options for linear gingival erythema should be standard periodontal therapy plus adjunctive therapies (10% povidine iodine or 0.12%-0.2% chlorhexidine) and consideration of the use of antifungals or antibiotics.[34] If the dentist feels inadequately equipped to handle HIV-associated periodontitis or fails to control the disease, then referral is required.

Referral can be made to:

- Periodontists
- General practice dentists with a high HIV case load or an interest in HIV infection
- Specialised clinics at major hospitals.

Dental management

- Chlorhexidine 0.12% - 0.2% mouthwash, 15 mL rinsed in the mouth for 1 minute 8 to 12 hourly.[35] (Note: chlorhexidine used over prolonged periods may cause discolouration of teeth and restorations).

AND

- Metronidazole 400 mg (child 10 mg/kg up to 400 mg) orally, 12 hourly for 5 days.[35]

Non-Periodontal Infections

Syphilis

Syphilis is caused by the bacterium *Treponema pallidum*, subspecies *pallidum*. Syphilis causes primary, secondary and tertiary disease. Atypical presentations of syphilis are common. The primary lesion of syphilis develops after a few weeks and is characterised by the chancre, which presents as an asymptomatic, clean-based, shallow but indurated ulcer.[45] Chancres may be found in the mouth and are sometimes associated with regional lymphadenopathy.[45] The secondary manifestations of syphilis take a few months to develop and most commonly involve a systemic rash and lymphadenopathy. Oral features include diffuse erythema or mucous patches which fuse to form snail track ulcers. Tertiary syphilis can present as neurosyphilis, cardiovascular syphilis and gummas. Gummas may occur in the mouth and the lesions range in size from microscopic to a number of centimetres in diameter. Gummas are chronic, asymptomatic, indurated nodular or ulcerative lesions. Atrophic glossitis and syphilitic leukoplakia are other oral manifestations of tertiary syphilis. The significance of syphilis in the context of HIV infection is complex due to similarities in the manifestations of HIV and syphilis. However, treatment of syphilis, as well as other sexually transmissible infections, will decrease the transmission of HIV.

Tuberculosis (TB)

TB is caused by *Mycobacterium tuberculosis*.[46] The atypical mycobacteria are beyond the scope of this document. People with HIV infection may develop TB via primary infection, reactivation of latent infection and re-infection with new strains. TB is rare in Australian-born people but much more common in those born, or have lived, in countries of high TB prevalence.[46] TB may present as granulomas, which form chronic ulcers with a grey-yellow slough in the mouth. There may also be lymphadenopathy in the head and neck. TB can occur at any CD4 cell level, however the frequency and severity of disease is inversely proportional to the CD4 cell level. TB presents significant infection control issues if the patient has active disease.

Viral Infections

There are seven groups of viruses that commonly cause oral manifestations. Patients with HIV infection and co-infected with any of these viruses are at increased risk of developing oral conditions.[27] The viral groups in addition to HIV include herpes simplex virus (HSV 1 and 2), varicella zoster virus (VZV), cytomegalovirus (CMV), human papilloma virus (HPV many subtypes), Epstein-Barr virus (EBV), molluscum contagiosum virus 22 (MCV22) and human herpesvirus 8 (HHV8).[28] In a person with HIV infection, co-infection with these viruses may manifest in the oral cavity in a typical manner no different from the pattern of infection seen in an immunocompetent person. However, the infections are more likely to be unusual, severe, widespread and recurrent in people with HIV infection. Also, the viruses can also be involved in the formation of neoplasms and oral lesions that would be considered unconventional in an immunocompetent person. The prevalence of oral viral infections increases with reducing CD4 cell count.[14,18,21] The viral infections may be primary infections or a reactivation of latent infections due to reduced immune surveillance.[28] The oral manifestation of viral co-infections with HIV is discussed below. Treatment of viral infections, on the whole, should be done by a GP.

Herpes simplex virus (HSV)

HSV has two main types, type 1 and type 2. HSV when it appears on the lips is known as herpes labialis or a cold sore. Primary infection may be very severe whereas recurrent infections are usually less severe. Disseminated infection and herpes encephalitis is possible. In people with HIV infection, recurrent HSV infection is common.[47]

- **Description:** herpes labialis presents as multiple small vesicles or ulcers on the lips and may include adjacent skin. Intra-oral HSV infection presents as small, round vesicles that rupture, leaving shallow ulcers which can coalesce. The lesions are superimposed on an inflammatory, erythematous base
- **Location:** lesions occur on the lips and anywhere in the oral cavity. In the mouth, HSV is commonly found on keratinised epithelium, including hard palate, gingiva and dorsum of the tongue, but in people with HIV infection it can sometimes be found on non-keratinised epithelium[28]

- **Symptoms:** prodromal symptoms may be present. The lesions may give mild-to-severe pain. They may be localised or widespread, involving the entire oral cavity and lips. Fever, lymphadenopathy and other symptoms may occur especially with a primary infection
- **Duration:** rapid onset with a duration of 7–14 days
- **Diagnosis:** swab for PCR analysis.

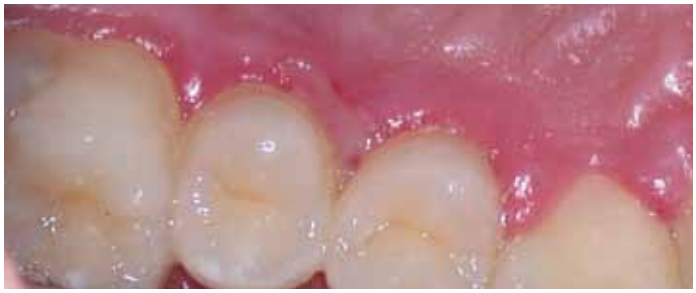

Figure 10: Herpes simplex virus lesions on the gingivae

Treatment for herpes simplex virus (HSV)

No treatment required if symptoms are mild. Severe or recurrent infections should be treated with topical and/or oral antiviral medications such as aciclovir, famciclovir or valaciclovir by a GP.

Varicella zoster virus (VZV)

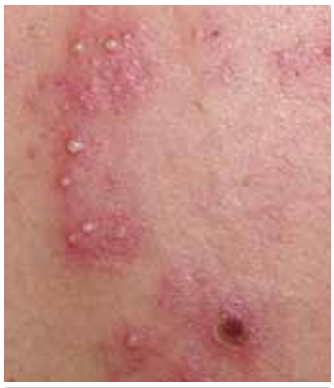

Figure 11: Varicella zoster virus vesicles on the skin

VZV is the herpes virus that causes the primary infection known as chicken pox and can reactivate from a latent state to cause herpes zoster (HZ) or shingles. The pattern of VZV infection is generalised in primary infection while HZ infection is usually unidermatomal but can be multidermatomal or disseminated.[28,47] VZV infection can be recurrent.[47]

- **Description**: intra-orally, VZV presents as a roughly linear eruption of herpetiform vesicles or bullae that ulcerate, and these may coalesce. Extra-orally, the vesicles can ulcerate and form a crust or scab. The vesicles or ulcers are bordered by erythema. The infection may leave scars
- **Location:** on the face and in the mouth, the distribution corresponds to a branch of the trigeminal nerve
- **Symptoms:** there may be prodromal symptoms present. The rash gives mild-to-severe pain
- **Duration:** usually 10 – 14 days but infections can become chronic
- **Diagnosis:** clinical, swab for PCR analysis if diagnosis uncertain.

Treatment for varicella zoster virus (VZV)

Urgent treatment is required with oral antiviral medications, such as aciclovir, famciclovir or valaciclovir to reduce illness severity and complications. Herpes zoster in the ophthalmic (V1) distribution of the trigeminal nerve requires ophthalmological referral to minimise ocular complications.

Cytomegalovirus (CMV)

In people with HIV infection, CMV can present with a wide array of complications such as gastrointestinal tract ulceration, hepatitis, encephalitis, retinitis, leukopenia and respiratory infections.[28,48] There is a relationship between CMV infection and xerostomia in people with HIV infection.[48] Relapse after treatment is common.[28]

- **Description:** CMV causes punched out ulcers from millimetres to several centimetres in diameter that can erode deep into tissues
- **Location:** mainly the palate or gingiva, but occasionally the buccal mucosa, tongue and pharynx are involved
- **Symptoms:** the oral ulcers can cause mild-to-severe pain and xerostomia
- **Duration:** variable
- **Diagnosis:** biopsy and culture may be used in diagnosis.

Treatment for cytomegalovirus (CMV)

Medical practitioners may prescribe antiviral medication such as ganciclovir or foscarnet to treat CMV infection.

Human papilloma virus (HPV)

A variety of benign mucocutaneous lesions are induced by the HPV, including verruca vulgaris, condyloma acuminatum, focal epithelial hyperplasia (Heck's Disease) and squamous papilloma. Verruca vulgaris is connected with HPV types 1, 2 and 7.[49] Condyloma acuminatum is associated with HPV types 6 and 11.[49] HPV types 13 and 32 are linked to focal epithelial hyperplasia.[49] HPV is linked with oropharyngeal squamous cell carcinoma.[47,50]

Verruca vulgaris

Verruca vulgaris, also known as the common wart, may present as multiple, large and disfiguring in conjunction with HIV infection, but most commonly the presentation is typical.[47]

- **Description:** single or multiple lesions of variable diameter. They may be sessile or pedunculated and are cauliflower-like growths with a white or pink surface
- **Location:** anywhere in the oral cavity but more commonly seen on the labial mucosa
- **Symptoms:** usually asymptomatic
- **Duration:** chronic
- **Diagnosis:** clinical, however biopsy is definitive.

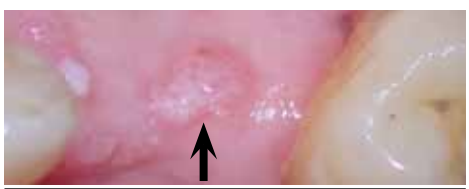

Figure 12: Verruca vulgaris (common wart) on the gingiva

Condyloma acuminatum

Condyloma acuminatum, also known as the venereal wart, is characteristically found on anogenital mucosa, however warts may also be seen on oral mucosa. Warts may present as multiple, large and disfiguring lesions in association with HIV infection.[47]

- **Description:** single or multiple lesions of varying sizes. They are soft and have a pink to dirty grey appearance. Often multiple nodules coalesce to form pedunculated or sessile papillary growths
- **Location:** they can be found on any mucosal surface, particularly the ventral tongue, gingiva, labial mucosa and palate
- **Symptoms:** normally asymptomatic
- **Duration:** chronic
- **Diagnosis:** clinical, however biopsy is definitive.

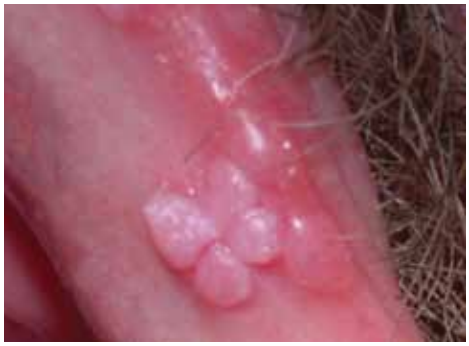

Figure 13: Condyloma acuminatum (venereal wart) on the buccal mucosa

Treatment for verruca vulgaris and condyloma acuminatum

Management can be by a general dentist with experience in this area. Otherwise referral to a GP, dermatologist, oral medicine specialist or oral and maxillofacial surgeon for treatment, if warranted.

Medical and surgical treatment may be appropriate depending on the site, characteristics and number.[49] Options include excision, electrosurgery, cryosurgery, CO_2 laser, topical podophyllin resin/interferon alpha injections,[49] podophyllotoxin, salicylic acid, tricholoracetic acid, bichloroacetic acid or imiquimod.[47]

Epstein-Barr virus (EBV)

EBV is also known as human herpesvirus type 4 (HHV4). EBV has been connected to infectious mononucleosis, Burkitt's lymphoma, non-Hodgkin's lymphoma and nasopharyngeal carcinoma.[28] The chief manifestation of EBV in people with HIV infection is oral hairy leukoplakia, and so EBV and oral hairy leukoplakia will be discussed together. EBV has been linked to oral ulceration in patients with advanced HIV infection.[51]

Oral hairy leukoplakia (OHL)

EBV is found mainly in B lymphocytes but also in epithelial cells and salivary glands tissue.[52] OHL is induced and maintained by repeated direct infection of the epithelial cells by EBV in the saliva[52] and is associated with EBV and immunosuppression. Rarely OHL has been reported in immunocompetent people without HIV infection.[53] OHL is increasingly found in patients with HIV infection as CD4 cell counts fall and is prevalent when below 150 cells/μL.[27] OHL may be considered a marker of disease progression.[19] Reported prevalences of OHL in untreated patients with HIV infection range from 0% to 24%,[14-16,21,54] however actual rates may be greater.[13,28] Modern therapies such as cART and topical treatments can reduce the prevalence of OHL in patients with HIV infection.[37,55] OHL may recur after stopping treatment.[56]

- **Description:** whitish, elevated, non-removable patch of variable size. Characteristically, the surface of the lesion has vertical ridges but smooth lesions can occur
- **Location**: lateral borders of the tongue and lesions may extend onto the ventral and dorsal surfaces of the tongue and occasionally on the buccal mucosa
- **Symptoms:** usually asymptomatic
- **Duration:** chronic
- **Diagnosis:** clinical.

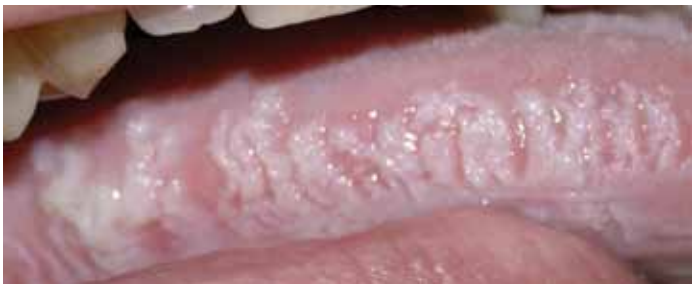

Figure 14: Oral hairy leukoplakia on the lateral surface of the tongue

Treatment for oral hairy leukoplakia (OHL)

Specific treatment is not indicated due to the benign and asymptomatic nature of OHL. It usually resolves following the introduction of effective antiretroviral therapy.

Molluscum contagiosum virus (MCV)

MCV is a poxvirus. There are four types of MCV, however MCV2 is responsible for orofacial disease in patients with HIV infection.[28] MCV is spread by direct skin-to-skin contact.

- **Description:** flesh coloured domes 2-6 mm in size but can be larger. The lesions have central umbilication
- **Location:** anywhere
- **Symptoms:** pruritis can be a symptom
- **Duration:** infections last months but can become chronic
- **Diagnosis:** clinical, biopsy rarely required.

Treatment for molluscum contagiosum virus (MCV)

Usually responds well to cryotherapy but other treatments such as curettage, cantharidin and imiquimod can be tried. Refer to a GP for treatment.

Human herpes virus (HHV)

HHV type 8 infection has been implicated in oral ulceration in patients with HIV infection.[51] HIV infection in conjunction with HHV8 infection has a strong association with the development of Kaposi's sarcoma (KS; see below). HHV8 is transmitted by exposure to contaminated body fluids.

Oral neoplasias

There are two common malignancies associated with HIV infection that may have oral involvement: KS and non-Hodgkin's lymphoma (NHL). KS and NHL were the most common forms of cancer associated with HIV infection in the pre-antiretroviral era; however today, cancers not associated with advanced HIV infection are more prevalent than KS and NHL.[57] At present there is insufficient evidence to establish a direct relationship between oral squamous cell carcinoma and HIV infection, however there are a limited number of case reports suggesting a connection between the two diseases.[13]

Kaposi's sarcoma (KS)

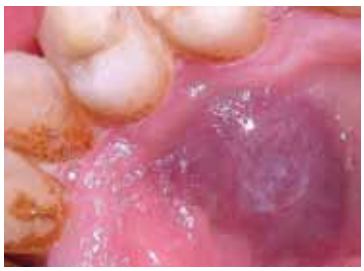

Figure 15: Kaposi's sarcoma

KS was the most common malignancy associated with HIV infection,[58] however, rates have significantly decreased with cART.[59] In 22% of cases, oral manifestations are the initial presentation and a majority will have oral involvement at some point.[58] KS is an endothelial cell malignancy associated with HHV8 and HIV infection.[60] There are a number of different forms of the disease but all are believed to represent aspects of the same pathological process. KS starts initially as an asymptomatic red macule which enlarges to form a red-blue plaque and these plaques may grow into lobulated nodules that may ulcerate and sometimes cause pain.

- **Description:** KS presents as pigmented lesions that range from flat macules to ulcerated nodular masses. The lesions can be red, purple, blue or brown in colour
- **Location:** the skin or mucous membranes can be affected. Most commonly the hard palate is involved, followed by the gingiva and buccal mucosa
- **Symptoms:** lesions are usually painless
- **Duration:** chronic without treatment
- **Diagnosis:** clinical followed by biopsy.

Treatment for Kaposi's sarcoma (KS)

Any treatment of intra-oral KS should be undertaken only in conjunction with the patient's medical specialist as many treatment options for the patient will need to be discussed. Any decision to biopsy these lesions should be made only in conjunction with the medical specialist as they are extremely vascular lesions and post-operative haemorrhage is a biopsy-related complication. Often commencement of cART can lead to spontaneous resolution of these lesions. Systemic chemotherapy, intra-lesional chemotherapy and radiotherapy are treatment modalities that may be employed. However, it should be realised that there can be many oral complications of radiotherapy and chemotherapy.

Non-Hodgkin's lymphoma (NHL)

Rates of HIV-associated NHL decreased with cART, however overall rates of NHL have continued to rise as a large proportion of NHL is not related to advanced HIV infection and background levels of this malignancy are increasing.[50] HIV infection in association with EBV can induce NHL. AIDS-related NHL is B-cell derived, while 70% of cases are systemic and 30% primarily involve the central nervous system.[61] Presentation varies according to histological type and extra-nodal involvement is common.

- **Description:** diffuse, rapidly proliferating, slightly purplish mass
- **Location:** in the mouth, the palatal-retromolar complex is commonly affected
- **Symptoms:** generalised symptoms (B-symptoms) of fever, night sweats and weight loss
- **Duration:** chronic without treatment
- **Diagnosis:** clinical followed by biopsy.

Treatment for non-Hodgkin's lymphoma (NHL)

Referral to appropriate medical specialists for consideration of treatment options. These may include surgical resection, chemotherapy, radiotherapy or palliation. It should be realised that there can be many oral complications of radiotherapy and chemotherapy.

Neurological conditions

There are many neurological conditions associated with HIV infection and cART. These conditions may have a direct or indirect impact on the oral cavity and include:

- Peripheral nerve neuropathies
  - Sensory neuropathy e.g. trigeminal neuralgia
  - Motor neuropathy e.g. facial nerve palsy
- HIV-associated neurocognitive disorders e.g. HIV-associated dementia.

Lesions of uncertain aetiology associated with HIV infection

Hyperpigmentation

In a review of seven studies, hyperpigmentation was found at a rate of 2.2%.[62] The exact cause of this low level of hyperpigmentation is uncertain, however it may be attributable to the combined effects of HIV infection and cART.

Aphthous ulceration

There are three types of aphthous ulcers: major, minor and herpetiform. The ulcers are of uncertain origin but immune mechanisms are implicated in the pathogenesis as well as local and general factors. The ulcers may be preceded by prodromal symptoms and may cause considerable discomfort. A biopsy of the ulcer to rule out infective causes is necessary before a diagnosis of aphthous ulceration can be confidently made.

Major aphthous ulcers

- **Description:** a number of ulcers greater than 10 mm in diameter which may heal with scarring
- **Location:** lips, cheeks, tongue, palate and pharynx
- **Duration:** more than 30 days.

Minor aphthous ulcers

- **Description:** a collection of ulcers less than 10mm in diameter which heal without scarring
- **Location**: lips, cheeks and tongue
- **Duration:** 1 – 2 weeks.

Herpetiform aphthous ulcers

- **Description:** larger numbers of ulcers that are 1-2 mm in diameter
- **Location:** lips, cheeks, tongue, palate, floor of mouth and pharynx
- **Duration:** 10 – 30 days.

Figure 16: Major aphthous ulceration

Treatment for aphthous ulceration

Dental management

- Topical anaesthetic agents can be used for mild lesions
- Topical corticosteroids
  - Triamcinolone acetonide 0.1% paste applied topically to the lesions three times a day after meals[35]
  - Betamethasone dipropionate 0.05% ointment applied topically to the lesion three times a day after meals[35]
- Nicotine lozenges or gum
- The use of chlorhexidine gel (Curasept™ gel) may improve comfort and aid healing.

Medical management

- Systemic corticosteroids
- Thalidomide use for severe ulceration, unresponsive to other treatments, requires medical specialist review.

Salivary gland dysfunction and xerostomia

2-10% of people with HIV infection are affected by xerostomia (dry mouth).[62] The cause of xerostomia is multifactorial and can include a CD8 lympho-cytosis syndrome related to HIV infection or side effects of medications or by opportunistic infections of salivary tissue. Enlargement of salivary glands occurs at a rate of less than 1% in adults but more commonly in children.[62] Saliva has many roles including: immune functions, lubrication, digestion and protection of the oral hard and soft tissues. Xerostomia can therefore reduce quality of life and lead to many dental complications. Xerostomia may be improved by:

- Frequent sips of water and keeping hydrated
- Sugar-free gum or lozenges to stimulate saliva flow
- Use of a saliva substitute
- Dental-care products designed for a dry mouth
- Referral to an oral medicine specialist for assessment of suitability for pilocarpine. Pilocarpine is a salivary stimulant which may provide some relief although there are risks of profound adverse effects[35]
- Consultation with treating GP to see if medications can be altered to improve the side effect profile.

Oral conditions associated with HIV treatment

Taste alteration

Multiple medications can often cause a taste disturbance. Consider recommending dental-care products designed for xerostomia.

Dry lips

Figure 18: Dry cracked lips

Associated with HIV-treatment, particularly the protease inhibitor, indinavir. The cracking and crusting of the lips can be extremely uncomfortable and unaesthetic. Protective creams designed for use on the lips, such as papaya-based lip ointments can be helpful in alleviating this condition.

Other conditions associated with HIV treatment include:

- Xerostomia
- Oral ulceration
- Erythema multiforme – Stevens-Johnson syndrome
- Lichenoid reactions
- Hyperpigmentation

There is the potential that many drugs prescribed by dentists may interact with cART. Therefore medications should always be prescribed in consultation with the patient's GP.

HIV and tooth decay

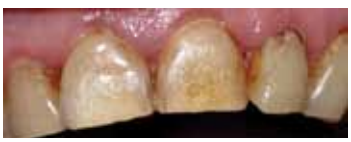

Figure 17: Early decay in a patient with HIV-related xerostomia

Dental caries can cause a significant burden of disease and affect quality of life for people with HIV infection.[63] Access to dental care improves oral hygiene and quality of life outcomes in people with advanced HIV infection or AIDS. Xerostomia is the most important factor in the development of dental caries that can be directly linked to HIV infection or its treatment. The most serious complication of dental caries is the occurrence of a potentially life-threatening infection, which is an important consideration in immunocompromised people.

Prevention of tooth decay

- Patient factors
  - Good oral hygiene
  - Consultation with a patient's GP to treat endogenous factors which may contribute to tooth decay:
    - Stomach acid from GORD
    - Medication side effects causing dry mouth.
- Dietary factors
  - Quality of diet e.g. sugar and acid
  - Quantity of food eaten
  - Frequency of eating
  - Sugar-free chewing gum.
- Dental factors
  - High fluoride dental-care products
  - Products containing CPP-ACP (casein phosphopeptide-amorphous calcium phosphate), such as Recaldent™ Tooth Mousse
  - Medicament trays to apply remineralisation products
  - Treatment of xerostomia with necessary dental care products
  - Regular dental check-ups.

Management of a suspicious sign or symptom indicative of HIV infection in a patient who has an unknown HIV status

- Review and recheck the medical history
- Advise the patient of
  - the presence of the lesion
  - the provisional diagnosis
  - the known association between the lesion and HIV infection or other conditions
- Explain to the patient that lesions associated with HIV can occur in non-HIV positive non-immunosuppressed people
- Offer appropriate treatment options if treatment is required immediately
- Recommend the patient visit his or her GP as soon as possible for pre-test counselling, a full check-up and an HIV test
- A referral letter should be given to the patient, and permission should be obtained to send a copy of the referral letter to the patient's GP*
- A referral letter should at least contain
  - patient details
  - examination findings
  - diagnosis
  - any treatment performed
- The patient should be advised that there is a potential for spread of HIV and that he or she should practise safe sex and avoid risk behaviours for HIV transmission
- Follow up with the patient after 7 days to ensure he or she has presented to a GP or sexual health clinic for an HIV test
- If the patient has a lesion that cannot be clinically diagnosed as an HIV- associated oral lesion and needs further investigation, refer the patient to an oral medicine specialist or an oral and maxillofacial surgeon. A referral letter should be given to the patient and permission should be obtained to send a copy of the referral letter to the specialist who will investigate the lesion*
- If possible, suggest to the patient that if the HIV test is positive, it may be beneficial to make a follow-up appointment with you to provide the opportunity to explain the influence of HIV infection on the mouth and the potential treatment needs
- If the patient returns with a positive HIV diagnosis and you do not feel qualified to manage the patient's dental requirements adequately, then consider referral options (see below).

** If the patient declines a referral for follow-up or to have a referral sent to a GP or specialist, then it is necessary to consult with a senior colleague and obtain a medicolegal opinion. There may be circumstances where a breach of confidentiality is legally permissible in order to have the patient adequately followed up.*

For advice, please contact the HIV/AIDS Legal Centre www.halc.org.au or (02) 9206 2060.

Management of an oral lesion associated with HIV infection in a patient with known HIV-positive status

- Advise the patient of the presence of the lesion and the potential diagnosis. If the lesion cannot be clinically diagnosed as an HIV-associated oral lesion, reinforce that the diagnosis is uncertain and needs to be confirmed
- Offer the patient treatment options if it is required immediately. Treatment should be initiated in consultation with the patient's primary GP and with input from specialists as necessary
- If the patient has a lesion that can be clinically diagnosed as an HIV-associated oral lesion, a letter should be written to the patient's GP outlining the diagnosis and treatment plan
- If the patient has a lesion that looks suspicious of an HIV-associated oral lesion, refer the patient to an oral medicine specialist or an oral and maxillofacial surgeon for assessment and diagnosis. A letter of referral must be written containing patient details, examination, diagnosis and treatment
- If you do not feel qualified to manage the patient's dental requirements adequately then consider referral options (see below).

For all patients with a suspected HIV-associated oral condition, regardless of HIV status

It is important to provide the patient with a sense of concern, support, understanding and care about his or her diagnosis. Reassure the patient about confidentiality and provide the opportunity for him or her to ask you questions and express his or her feelings about a potential diagnosis.

Monitor emotional response and offer support services through the AIDS Council within your State or Territory, or contact the Australian Federation of AIDS Organisations (AFAO) for assistance with social support on (02) 9557 9399.

A team approach should be adopted for any HIV-associated oral manifestation.

The patient's rights regarding disclosure

People with HIV infection are not required by law to disclose their HIV status to dentists, doctors or any other health professionals. People with HIV infection are encouraged to consider disclosure if they are having a medical examination, treatment or procedure as there is the potential that their HIV medications and related conditions may affect the medical management.[64]

The HIV/AIDS Legal Centre recommends that people with HIV infection carefully consider their decision to disclose their status to their dentist as there has been a history of patients experiencing stigma and discrimination following disclosure.[64]

Dentists and all other health-care professionals have a duty under the relevant state, territory or Commonwealth Privacy Act to ensure confidentiality is maintained should a person disclose his or her status. Also, all health-care professionals are bound by legislation that makes it illegal to discriminate on the basis of HIV status.

As dentists should maintain standard infection control procedures at all times, a person's HIV status should have no influence on a dentist's level of precaution or infection control practices.

Risk and management of occupational exposure

Occupational transmission of HIV from a patient to a dentist is very rare[65] and there are a number of potential risk factors associated with increased transmission.

…continued on page 12

ASHM resources

Other ASHM resources are available from the ASHM website: **www.ashm.org.au/publications**

Profession Based Booklets

- An Overview of Hepatitis C: Clinical management in opiate pharmacotherapy settings
- Antenatal Testing and Blood-Borne Viruses (BBVs)
- Correctional Officers and Hepatitis C
- Dental Health and Hepatitis C
- General Practitioners and Hepatitis C
- General Practitioners and HIV
- Nurses and Hepatitis C
- Pharmacy and Hepatitis C
- Police and Blood-Borne Viruses
- Prehospital Care Workers and Blood-Borne Viruses

Factsheets

- Decision Making in Hepatitis B
- Hepatitis B Factsheet: for people newly diagnosed
- Hepatitis C in Brief – patient factsheet
- Hepatitis C Management and Treatment for Clients of Pharmacotherapy Sevices
- HIV Patient Fact Sheet

Monographs

- ASHM Directory of HIV, Viral Hepatitis and Sexual Health Services
- B Positive: all you wanted to know about hepatitis B – a guide for primary care
- Co-infection: HIV & viral hepatitis – a guide for clinical management
- Hepatitis C: clinical management in opiate pharmacotherapy settings
- HIV and Viral Hepatitis C: policy, discrimination, legal and ethical issues
- HIV Management in Australasia: a guide for clinical care
- HIV, Viral Hepatitis and STIs: a guide for primary care

Distance-learning Kit

- Clinical Science of HIV Medicine CD

Manuals

- Australasian Contact Tracing Manual
  Available in hardcopy and online at www.ashm.org.au/ctm

Online resource

- Guide to Australian HIV Laws and Policies for Healthcare Professionals. Available online only at www.ashm.org.au/HIVlegal

Detailed References

Detailed references are available on the ASHM website at www.ashm.org.au/publications

Supporting Resources

Australasian Society for HIV Medicine. **HIV patient fact–sheets.** Darlinghurst: Australasian Society for HIV Medicine, 2008. Available at: www.ashm.org.au/hiv-patient-sheet

Bradford B, Dore G, Grulich A, Kidd M, Hoy J, McCoy R, et al, editors. **HIV, Viral Hepatitis and STIs: a guide for primary care.** Darlinghurst: Australasian Society for HIV Medicine, 2008. Available at: http://www.ashm.org.au/HIVhepSTIs

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Therapeutic Guidelines Limited. **Therapeutic Guidelines; Oral and Dental.** Melbourne: Therapeutic Guidelines Limited, 2007.

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Continued from page 11…

If a health-care worker has a needlestick injury from an HIV-positive patient, the following action should be taken:

- Wash injury or exposed membrane thoroughly with soap and water (an antiseptic could also be used on the skin). Do not use abrasive chemicals or implements that may damage the skin further.
- Seek medical advice immediately for assessment of the nature of the exposure, testing if appropriate, risk of transmission and the need for HIV post-exposure prophylaxis (PEP). PEP is a short course of HIV medication taken within 72 hours of exposure. **Specific advice can be obtained from: Needlestick Hotline, 24 hours a day: 1800 804 823.**

Referral pathways

- Referral options should be offered and discussed
- Explain to the patient why referral is necessary
- For medical practitioners with an interest in HIV, contact ASHM: (02) 8204 0700
- For dentists with an interest in HIV, contact the AIDS Council in your State or Territory, or the Australian Federation of AIDS Organisations: (02) 9557 9399
- For oral medicine specialists, oral and maxillofacial surgeons or periodontists, contact the Australian Dental Association: (02) 9906 4412.

Online Learning Module

An accompanying online education module covering the most important aspects of this printed resource and incorporating interactive self-assessment activities has been developed. For further information or to access this online education module visit the Australasian Society for HIV (ASHM) website at **www.ashm.org.au/e-learning**.

Contacts

General Contacts	Professional Bodies
Australasian Society for HIV Medicine (ASHM) T 02 8204 0700 W www.ashm.org.au	Australasian Chapter of Sexual Health Medicine (AChSHM) T 02 9256 9643 W www.racp.edu.au/page/australasian-chapter-of-sexual-health-medicine/
Australian Department of Health and Ageing (DoHA) T 02 6289 1555 W www.health.gov.au	Australian College of Rural and Remote Medicine T 07 3105 8200 or 1800 223 226 (Freecall) W www.acrrm.org.au
Australian Federation of AIDS Organisations (AFAO) T 02 9557 9399 W www.afao.org.au	Australian Dental Association (ADA) T 02 9906 4412 W www.ada.org.au
HIV/AIDS Legal Centre (HALC) T 02 9206 2060 or 1800 063 060 (Freecall) W www.halc.org.au	Royal Australian College of General Practitioners (RACGP) T 03 8699 0414 or 1800 331 626 (Freecall) W www.racgp.org.au
Ministry of Health – New Zealand T 0011 64 496 2000 W www.moh.govt.nz/moh.nsf	Royal Australian College of Physicians (RACP) T 02 9256 5444 W www.racp.edu.au
National Association of People Living with HIV/AIDS (NAPWA) T 02 8568 0300 or 1800 259 666 (Freecall) W www.napwa.org.au	Royal College of Pathologists of Australasia T 02 8356 5858 W www.rcpa.edu.au
National Serology Reference Laboratory (NRL) T 03 9418 1111 W www.nrl.gov.au	

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Dentists and HIV
DETAILED REFERENCES

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