Sexually transmitted infections, human immunodeficiency virus infection, and their manifestations in the oral cavity

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ABSTRACT  Manifestations of sexually transmitted infections are common in the oral cavity, and hence of significant interest to oral health practitioners. This paper reviews common sexually transmitted infections and how they can involve the oral cavity. This review covers viruses such as human immunodeficiency virus, the hepatitis viruses, herpes-viruses (herpes simplex, cytomegalovirus, Epstein-Barr), human papillomaviruses, and molluscum contagiosum. Also discussed are bacterial infections such as chlamydia, gonorrhea, group B streptococci and syphilis, protozoa and yeasts (Trichomonas and Candida). Typical presentations, their role in the oral cavity, and significance to dentists are considered.

Introduction

We have previously reported 10 common myths regarding sexually transmitted infections (STIs) [Table] 1. One of the most common is that STIs are strictly genital diseases 1. In fact, almost all have extragenital manifestations, which affect the oral cavity, eyes, cutaneous apparatus, cardiovascular system, neurological system, gastro-intestinal tract, hepatobiliary system, and musculoskeletal system.

Extragenital manifestations appear in the course of common STIs, may be directly related to human immunodeficiency virus (HIV) infection, or to congenitally acquired STIs. Some are only seen in immunocompromised patients. A multidisciplinary approach is ideal in order to arrest the relentless rise in the rate of STIs (including HIV) in the 21st century. In the United States, dentists are legally required to report the diagnosis of certain STIs 2. Sexually transmitted infections such as HIV can be transmitted from patients to dental surgeons and their allied professionals through accidental injuries in the course of dental procedures. Increasing awareness of STIs by dental surgeons is important for the welfare and protection of their patients, their contacts, as well as the

Table Sexually transmitted infections (STIs)—10 common myths 1

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<tr>
<td>1.</td>
<td>There is no difference between HIV and AIDS</td>
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<td>2.</td>
<td>Genital herpes is only caused by herpes simplex virus type 2</td>
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<td>3.</td>
<td>With new antiviral therapies, genital herpes is now a curable disease</td>
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<td>4.</td>
<td>If I have sex when I do not have visible genital warts, I will not infect my partner</td>
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<td>5.</td>
<td>Most cases of male urethritis are caused by gonorrhea and can be cured with a single injection</td>
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<td>6.</td>
<td>The female equivalent of male urethritis is urinary tract infection</td>
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<td>7.</td>
<td>Hepatitis B and C viruses are transmissible by sex; hepatitis A is not</td>
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<td>8.</td>
<td>The STIs are adult stuff, they do not affect infants and children</td>
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<td>9.</td>
<td>The STIs are strictly genital diseases</td>
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<td>10.</td>
<td>Genital rash or genital mass denotes an STI</td>
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dentists themselves and their associated oral health care professionals.

Viral infections

Human immunodeficiency virus

The HIV-AIDS pandemic is of great concern to all health professionals. In HIV-infected individuals, opportunistic infections present as the immunity declines. The most important mode of HIV transmission is sexual and unsafe sexual practices increase the risk. Mother-to-child transmission, intravenous drug abuse, and transfusion of infected blood and its products are the other modes of acquiring the disease. The oral manifestations of HIV can be conveniently categorized as: infections, neoplasms, immunologic disorders, and miscellaneous.

Infectious manifestations are most frequently due to fungal, bacterial, and viral agents and often give rise to a clinically diagnostic appearance. They include: oral candidiasis, painful gingivostomatitis (bacterial or largely immunological), bacillary angiomatosis, herpes simplex, cytomegalovirus (CMV), hairy leukoplakia, Kaposi's sarcoma, oral lichen planus, and lymphoma in that order.

Candidiasis is the most common opportunistic infection presenting in the oral cavity of HIV-infected persons. This condition is discussed in more detail later, in the section on yeast and protozoal infections.

Human immunodeficiency virus is an important cause of recurrent painful gingivostomatitis, giving rise to multiple bouts of aphthous stomatitis (an immune-mediated disorder), or a necrotizing bacterial periodontitis. The latter is associated with pain, edema, erythema, and local tissue destruction. Linear erythematous marginal gingivitis is another association, but is comparatively benign, being responsive to topical antiseptic gargles such as chlorhexidine gluconate.

Bacillary angiomatosis manifests as a soft mass or erythematous papules, which bleed if touched and is often confused clinically with Kaposi’s sarcoma. Rochalimaea henselae is the responsible pathogen. Both Kaposi’s sarcoma and bacillary angiomatosis are sometimes associated with a black hairy tongue (Figure 1).

Mucosal tuberculosis is known to occur in HIV-infected patients and may present as chronic progressive ulceration of the oral mucosa.

Herpes simplex virus (HSV) infections around and within the oral cavity is common in HIV disease. Verrucous lesions of human papillomavirus (HPV) and papular lesions of molluscum contagiosum are frequently evident in homosexuals with HIV.

Cytomegalovirus infection may present as solitary, deep ulcerations on the buccal and labial mucosa. The appearance is non-specific and indistinguishable from other causes of HIV infection—associated oral ulcers (extragenital syphilitic chancre, major aphthous stomatitis, cryptococcosis, and histoplasmosis). However, early diagnosis of CMV is very important, because of its devastating potential for dissemination to the retinæ, meninges, and other organs. Tissue biopsies and cultures are therefore essential prerequisites for an accurate diagnosis.

Oral hairy leukoplakia consists of adherent, corrugated white patches typically affecting the lateral parts of the tongue. They are said to be caused by Epstein-Barr virus (EBV) and are regarded as pathognomonic of HIV-induced decline in the CD4 count to below 200 /mm³.

Kaposi’s sarcoma is the most common oral cavity malignancy in HIV disease and is a hallmark of immune deterioration, which appears to be mediated by a human herpesvirus type 8. Clinically, it presents as red to blue macules, papules, nodules or ulceration on the palate, but diagnosis requires histopathological confirmation.

Oral lichen planus is an inflammatory disorder, at times difficult to distinguish from leukoplakia and can be resistant to therapy when associated with HIV. Non-Hodgkin’s lymphoma, xerostomia, and parotitis are other uncommon oral manifestations of HIV.

Most HIV-infected persons have oral manifestations, during some part of their illness and may even be the presenting feature. A high index of suspicion is therefore necessary, for example, when dealing with a previously healthy young adult with oral candidiasis. It is also important for dentists to be aware of the differing oral presentations of HIV that prevail in their own locality. Suspicion of HIV on clinical grounds is a matter of great concern to dentists; during dental procedures due precautions must be taken to avoid any possible risk of transmission to others. A protocol for the prevention and initial management of persons with needlestick injuries should be established.
Herpes simplex viruses

Herpes simplex virus types 1 (HSV-1) and 2 (HSV-2) are two of the eight human herpesviruses, all of which can establish latency in the human host and are globally endemic. The prevalence of such infections varies worldwide; in developed countries it ranges from 15% to 70% for HSV-2 \(^6-8\) and 35%-80% for HSV-1 \(^9\).

In Hong Kong, the seroprevalence of HSV-2 antibodies in STI clinic attendees reached 24% in males, 36% in females, and 78% in high-risk groups such as female sex workers \(^10\). In the general population, 18% of those aged >24 years had evidence of past infection \(^10\).

Both HSV-1 and HSV-2 can infect the genital area, clinically manifesting as genital herpes, as well as the orolabial area, presenting typically as “cold sores” or “fever blisters” (Figure 2). Though differences between HSV-1 and HSV-2 are subtle and clinically they are indistinguishable, HSV-1 tends to favor orolabial sites and HSV-2 the genital region. Recurrent orolabial infection is almost always due to HSV-1. Orolabial infections can be transmitted both to and from the genital region via direct skin contact during oral sex, direct contact with an infected orolabial lesion or via infected oral secretions. Most HSV-1 transmissions occur during childhood, when there is a greater chance of contact with infected oral secretions and person-to-person contact. While the condition is most infectious if there are active lesions, viral shedding and transmission may occur at other times, and particularly when the patient has a common cold or following oral trauma \(^11\).

Primary infection at an orolabial site is usually asymptomatic, but may result in an extremely infectious, self-limiting gingivostomatitis. This commonly ensues in small children and infants for whom treatment is mostly supportive (mouthwashes and analgesia) but often entails antiviral agents. Primary HSV-1 infection in adolescents typically presents as ulcerative pharyngitis. Following primary infection, latency is established in ganglia of the trigeminal, facial and/or vagus nerves. Recurrent herpes
labialis is estimated to occur in 20%-40% of those infected; only 1% experience severe symptoms.  

While primary infection may present with intraoral, pharyngeal, and labial lesions in the immunocompetent hosts, intraoral recurrences are rare due to protective enzymes in saliva. Most symptoms present labially. Recurrences may be frequent and painful and associated with significant psychological distress. Triggers associated with recurrences include UV light, febrile illnesses, stress, menstrual cycle, and surgical procedures including dental surgery. Approximately 50% of recurrences are preceded by prodromal symptoms such as itching, burning, and redness. Lesions may then appear, usually on the vermilion border of the lips. These progress to ulcers and crusted lesions, with complete healing by day 10.

**Human papillomavirus**

There are over 100 types of HPV, which may generally be categorized as those causing STIs (anogenital and mucosal infections), nongenital cutaneous infections, and epidermodysplasia verruciformis. Anogenital diseases caused by HPV include condyloma acuminata (genital warts), Bowenoid papulosis, Bowen disease, intra-epithelial neoplasia, and carcinomas of the vulva, vagina, cervix, anus, and penis. Human papillomavirus causes lifelong, asymptomatic, and subclinical infections. Virus shedding is present even for asymptomatic hosts. Thus it is likely that during most sexual transmission transactions, the donor partner is asymptomatic (has subclinical disease).

In the oral cavity, HPV types 16 and 18 infections (with relatively high carcinogenic potential) are associated with lichen planus, oral leukoplakia, and oral carcinoma. Human papillomaviruses 6 and 11 (the most common types causing condyloma acuminata and having low carcinogenic potential) are associated with laryngeal papilloma. Whereas HPV types 16 and 18 are also associated with laryngeal carcinoma.

The most common HPV types in Hong Kong are HPV 16 and HPV 52, followed by HPV 58 and HPV 18. In general, the prevalence rates are high (around 20%) in younger age-groups (between 20 and 30 years), but decline to below 10% in those 40 to 50 years and a second peak ensues in older people (aged 50 to 60 years).

It is possible that sexual behavior could be relevant to the oral manifestations of HPV, but the issue is still controversial. A difficult scenario to deal with is the child with oral condyloma acuminata. Sexual abuse must be excluded, although maternal transmission is theoretically possible. If a dentist ever encounters such a child, immediate measures to protect the child and recourse to suitable advice and support services become imperative.

**Molluscum contagiosum virus**

Molluscum contagiosum virus types 1-4 cause the self-limiting skin disease molluscum contagiosum. Lesions are small, discrete, and dome-shaped papules with characteristic umbilication, and those in the anogenital region are believed to be sexually transmitted.

Molluscum contagiosum can also occur as oral and perioral lesions, particularly in HIV-infected individuals. The route of transmission of such lesions is still controversial. If intraoral molluscum contagiosum is suspected, the diagnosis needs histopathological confirmation, followed by referral to a medical practitioner for HIV pre-test counseling.

**Hepatitis viruses**

Hepatitis B, C, and D viruses are sexually transmissible in heterosexual relationships. Hepatitis A, B, C, and D viruses can be transmitted by male homosexual behavior. Sexual transmission is well documented for hepatitis viruses A and B. The rate of sexual transmission for hepatitis C is likely to be low. Hepatitis D can only co-exist with hepatitis B. There is no definite evidence that hepatitis E is sexually transmissible. Hepatitis G, GB, and TT may be sexually transmissible. However, their significance as disease-causing viruses is unknown.

As dentists are performing invasive procedures, hepatitis B and C viruses transmitted from patients to dentists are genuine concerns. Dentists should therefore regard all patients as potentially high-risk, as many individuals are not aware that they were ever infected and could be carriers of these viruses. The Centers for Disease Control and Prevention currently recommends that dental practices develop a written policy on immunizing relevant workers and referring personnel to appropriate professionals to be considered for vaccination. Similarly, consideration should be given to developing a corresponding written protocol for needle-prick and kindred injuries in dental practices.
**Epstein-Barr virus**

Epstein-Barr virus is a member of the herpesvirus family. Primary infection gives rise to the clinical syndrome of infectious mononucleosis and usually occurs in adolescents and young adults. Typical symptoms include fever, sore throat, and cervical lymphadenopathy; this syndrome is followed by latent, lifelong infection of lymphocytes and epithelial cells. The virus is carcinogenic and chronic infection may lead to nasopharyngeal carcinoma or Burkitt’s lymphoma. Increasingly convincing evidence suggests that a minority of individuals could have acquired their primary EBV infection through sexual transmission.\(^{23-26}\)

In the oral cavity, infectious mononucleosis usually manifests as pharyngitis, palatal petechiae, and tonsillar enlargement. When a dentist sees an adolescent or young adult with palatal petechiae, the patient should be referred to a medical practitioner for clinical and serological confirmation of primary EBV infection.

**Cytomegalovirus**

Like EBV, CMV is a herpesvirus, causing primary infection followed by lifelong latent infection. Primary infection simulates the infectious mononucleosis syndrome, with fever, malaise, pharyngitis, and sometimes, cervical lymphadenitis. Cytomegalovirus causes generalized infection in almost every organ system in immunocompromised patients such as those with HIV. It also gives rise to congenital infection. Indirect epidemiological evidence suggests that CMV too can be transmitted via sexual contact.\(^{27-29}\)

Cytomegalovirus infection in immunocompetent hosts is usually not a concern for dentists. In the oral cavity of such patients, it may give rise to stomatitis, oral ulceration, and pharyngitis, whilst esophageal involvement can lead to dysphagia.

**Bacterial infections**

**Chlamydia trachomatis**

*Chlamydia trachomatis* serovars A-C causes trachoma, a chronic eye disease. *Chlamydia trachomatis* serovars D-K are sexually transmitted and cause genital infections including urethritis and epididymitis in men and endocervicitis and pelvic inflammation in women. *Chlamydia trachomatis* serovars L1-L3 cause lymphogranuloma venereum, a tropical STI.  

*Chlamydia trachomatis* can be transmitted by oral sex; the pharynx being an important site for colonization (mainly of serovars D-K). According to statistics from the Public Health Laboratory Service in Hong Kong, out of a total of 15,533 received from the Social Hygiene Clinics in 2004, 17.5% of relevant samples tested positive for chlamydia [personal communication]. Most women and many men with *C. trachomatis* serovars D-K genital infection are asymptomatic, though they may eventually suffer significant long-term sequelae, including infertility.

The prevalence of detectable chlamydia in the pharynx ranges from 1.4% in men who have sex with men to 22.5% in female sex workers.\(^{30}\) The clinical significance of pharyngeal *C. trachomatis* carriage is still controversial. Doctors treating patients with pharyngitis would not usually investigate for possible *C. trachomatis* infection, nor would they routinely investigate for pharyngeal carriage when dealing with suspected or confirmed *C. trachomatis* genital infection. Thus, with the exception of dentists in academic settings, the pharyngeal carriage of *C. trachomatis* has not been a concern for most dentists.

**Neisseria gonorrhoeae**

The obligate human intracellular pathogen *Neisseria gonorrhoeae* is the causative organism of an STI. Typically the organism occurs genitally, in the cervix and urethra. Infections may also occur in the anorectum and pharynx and may disseminate. In adults, only mucus membranes lined with columnar or cuboidal cells are susceptible. Thus, pharyngeal carriage poses little threat of transmission to the dentist.

Oral manifestations may result from direct inoculation during orogenital sex; pharyngeal infection being the most common. Pharyngeal infection is more liable to be transmitted via fellatio (oral stimulation of the penis) rather than cunnilingus (oral stimulation of the vulva), and as such the highest rates occur in men who have sex with men and heterosexually active women. While reported symptoms include acute pharyngitis or tonsillitis occasionally associated with fever and lymphadenopathy, it is asymptomatic in over 90% of cases.\(^{32}\) The prevalence of oral gonorrhea varies widely.\(^{33}\) For individuals with gonorrhea, pharyngeal infection can occur in up to 3%-7% of heterosexual men; 10%-20% of heterosexual women, and 10%-25% of homosexual men.\(^{33}\) The lesions
are non-specific and may mimic other oral infections including HSV. Symptoms may vary from mild erythema to severe ulceration, burning or an itch that may impede oral function.

Management of gonorrheal infections involves treatment with appropriate antimicrobial agents. Other STIs should be screened for and all sexual contacts tested and treated as appropriate.

**Syphilis**

Syphilis is a systemic chronic infection caused by the spirochete *Treponema pallidum*. It is usually transmitted by sexual contact. The incubation period is variable from 9 to 90 days. Clinical manifestations vary according to the stage—early (less than 2 years of duration; involves primary and secondary stages) and late (more than 2 years duration and commonly latent, in which case only serological investigations can detect the disease).

Primary syphilis is characterized by a single, painless, indurated ulcer (primary chancre) with non-tender regional lymphadenopathy. It is commonly encountered on the penis of infected men and genitilia of infected women. It may occur in the oral cavity, especially in homosexual men. In the secondary stage there are symmetrical mucocutaneous, pink-red maculopapular eruptions on the trunk and extremities, typically involving the palms and soles. Condyloma lata (Figure 3) are moist hypertrophic papular lesions occurring in the genital regions. The oral mucosa often reveals presence of mucous patches, which form circumscribed, superficial mucosal erosions or plaques (Figure 4). Sometimes, linear erosions may be noted as snail track ulcers. Late syphilis is typically asymptomatic. Late (or tertiary) syphilis, the sequel of untreated early syphilis, may be asymptomatic but may manifest as deep-seated punched-out painless ulcers (or gumma), which commonly involve the skin and musculoskeletal system, but can affect almost any organ. In the oral cavity, gummatous lesions can result in palatal perforation.

The identification of mucous patches is vital, as they indicate the presence of active syphilis; the lesions are teeming with the spirochetes and highly infectious. Hence, due precautions by the dentist are critical.

Congenital syphilis implies vertical transmission from a mother to fetus possibly during the second trimester of pregnancy. The term “snuffles” refer to the highly infectious nasal discharges encountered in newborns with syphilitic mucositis. Teeth are typically affected in congenital syphilis, resulting in so-called “Hutchinson’s teeth” that are characteristically peg-shaped, notched, and widely spaced upper central incisors and “mulberry molars”, with multiple, poorly developed cusps. Rhagades are linear scars at the angles of mouth.

Chronic atrophic glossitis and leukoplakia due to syphilis may be confused with similar appearances in candidiasis/HIV infection. High-arched (gothic) palate and maxillary hypoplasia (bulldog jaw) may occur with saddle nose deformity and may first be noticed by dentists.

Upon referral, the diagnosis of early disease is based on identifying classical clinical features, and confirmatory dark ground illumination, as well as Venereal Disease Research Laboratory or rapid plasma reagin tests. More specific confirmatory tests such as Treponema pallidum immobilization and hemagglutination tests as well as the fluorescent treponemal antibody testing may be carried out in institutes with the appropriate facilities.

Syphilis dramatically responds to parenteral penicillin. Patients sensitive to penicillin may need erythromycin or tetracyclines. Early identification and treatment prevents delayed systemic (cardiovascular and neurological) complications as well as gumma.

**Group B streptococci**

Group B streptococci commonly colonize the vagina. In immunocompromised patients, generalized infection may lead to pneumonia, meningitis, bacteremia, osteomyelitis, septic arthritis, and urinary tract infection. In pregnant women they may cause chorioamnionitis, neonatal sepsis, and pelvic inflammation after delivery.

Group B streptococci colonize the oral cavity. However, the clinical significance of asymptomatic colonization is still unknown. It is hypothesized that group B streptococci can be transmitted via sexual contact and fecal-oral routes. At present, the sexually transmissible potential of group B streptococci and its significance are not concerns for dentists practicing outside academic settings.

**Yeast and protozoal infections**

**Candidiasis**

*Candida* spp (mainly *Candida albicans*) are yeast-like fungi.
They are normal commensals in the genitourinary and gastro-intestinal systems that may become opportunistic pathogens. The importance of sex as a possible route of transmission is debatable. In most women vulvovaginitis due to candida is not likely to be related to sexual transmission. In men with balanitis or balanoposthitis due to *C. albicans*, a sexual route of transmission is possible but also not obligatory.

*Candida* spp causes oropharyngeal and esophageal infections (Figure 5). Oropharyngeal candidiasis can manifest as: membranous, erythematous, chronic atrophic and angular cheilitis types. Sexual transmission of oropharyngeal candidiasis has been documented in patients with HIV infection. In immunocompetent individuals, clinical oropharyngeal candidiasis is far less common. Linear erythematous gingivitis (LEG) is fairly common in HIV infection. It might be associated with candidiasis. However, according to our experience, in many cases there is no evidence of oral candidiasis and in a significant proportion of patients it may not clear even after sufficient anti-candidal therapy. Hence, we believe, LEG

* Figure reproduced from Dermatol Online J 2005;11:46
should be investigated further if it does not respond to antifungal therapy.

Dentists may come across many patients with oropharyngeal candidiasis, some with obvious precipitating factors such as diabetes mellitus, and some without. Sexual behavior (including oral sex) is unlikely to be a significant factor for most patients.

**Trichomonas vaginalis**

*Trichomonas vaginalis* is a trophozoite, transmitted via sexual intercourse. It mainly causes vulvovaginitis in women and balanitis and urethritis in men. The oral cavity can be infected by other species of *Trichomonas*, mainly *Trichomonas tenax*, which is not an STI. Thus, for all practical purposes, *T. vaginalis* infections do not pose a concern for the dentist.

**Discussion**

Sexually transmitted infections are not restricted to genital areas. As an important sexual organ, the mouth is vulnerable to STIs. Dentists have an important role in identifying such diseases early and referring suspected patients for further investigation and management. This will reduce the risk of complications, the risk of further transmission to sexual partners, as well as direct and indirect costs to individuals and to society. Dentists are also in an ideal position to give preliminary advice to patients on safe sex.

Oral manifestations may be indirectly related to sexual activity. We have previously reported that fixed drug eruptions can be precipitated by sexual activities. Sexually transmissible infections are not limited to HIV, syphilis, and gonorrhea. Microbes such as EBV and CMV are increasingly recognized as sexually transmissible. Indeed, there is no clear division between pathogens that are sexually transmissible and those that are not.

There are policy and research implications for the importance of STIs for dentists. Among our suggestions are a survey to explore knowledge, attitudes, and practice of dentists regarding STIs affecting the oral cavity. An assessment is warranted to examine the training needs of dentists to protect themselves and their staff from such diseases.

Owing to the constraints of space, we have not covered the enteric STIs, several other syndromes, and certain tropical disorders. Nor have we addressed the investigation and treatment of the individual STIs. Typically there are multiple investigative modalities for each sexually transmissible pathogen. Apart from medication, management of the individual relies on assessment and modification of risk behavior, contact tracing, investigations for other STIs, pre-test counseling, and appropriate immunization. A non-judgmental attitude and a commitment to promoting sexual health are the armaments of all health care professionals battling against STIs and HIV in the 21st century.

**Acknowledgments**

Figure 4 was originally published in the paper *Oral lesions of syphilis: an isolated, rare manifestation* (Dermatol Online J 2005;11:46), and is reproduced here with the permission of that journal. The Table, originally published in the *Australian Family Physician*, was reproduced with the permission of The Royal Australian College of General Practitioners.

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