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Mountain Plains AIDS Education and Training Center

HIV/AIDS in Dental Care

A Case-Based Self-Study Module for Dental Health Care Personnel

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LEARNING OBJECTIVES

By the completion of this module the learner will be able to:

- Communicate effectively with patients regarding HIV infection
- Assess risk factors for HIV infection
- Identify specific lesions associated with HIV/AIDS
- Describe basic treatments for oral lesions associated with HIV infection
- Determine need for consultation and referral related to HIV infection

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Overview of HIV Infection

Although the cause was unknown at the time, problems associated with the human immunodeficiency virus (HIV) were first noted in the United States in mid-1981 when the deaths of several young men living in metropolitan centers were reported to the Centers for Disease Control and Prevention (CDC). All of the men were diagnosed with a fatal pneumonia caused by *Pneumocystis carinii*, a common and rarely pathogenic fungus. Reports coming to the CDC from Los Angeles, New York, San Francisco, and other cities seemed to indicate that a sexually transmitted organism had affected the immune systems of these men. Further case reports showed that other infections and malignancies usually seen in persons with chronic, debilitating diseases and conditions causing immune dysfunction were also present. This syndrome of infection, immune suppression, and opportunistic diseases (infections and neoplasms) eventually became known as the acquired immune deficiency syndrome (AIDS) (CDC, 1992). Since 1981, HIV infection has become pandemic with over 30 million people infected worldwide (Libman & Makadon, 2000) and an estimated 40,000 new cases a year in the United States alone (CDC, 2001b).

In 1984 three independent laboratories identified the causative agent. A French team from the Pasteur Institute identified a retrovirus termed the lymphadenopathy-associated virus (LAV) and reported it as the causative agent for AIDS. In the United States, a team from the National Institutes of Health isolated a retrovirus, identified as the human T lymphotropic virus III (HTLV-III) and labeled it as the etiologic agent for AIDS. A team in San Francisco also isolated a retrovirus, AIDS-related virus (ARV), and designated it as the causative agent for AIDS (Little, Falace, Miller, & Rhodus, 2002). All were similar retroviruses, with minor differences in amino acid sequences. In 1986, the World Health Organization recommended that the virus be called the human immunodeficiency virus (CDC, 1991).

HIV is transmitted by sexual means, through the exchange of body fluids (especially infected semen during intercourse); by non-sexual means, via the parenteral transfer of infected blood; or through vertical transmission to infants born of infected mothers. The only fluids that have been demonstrated to be associated with transmission of the virus are blood, semen, breast milk, and vaginal secretions. Casual contact (shaking hands, hugging, casual kissing, etc.) has not been shown to transmit HIV (CDC, 2001a). Individuals who appear to be most susceptible to HIV infection are those with repeated exposures to the virus, other concurrent sexually transmitted infections (STIs), and immune systems that have been challenged by repeated exposures to various antigens (semen, hepatitis B, or blood products) (CDC, 1991). According to the CDC, of all AIDS cases reported by September 2001, sexual behavior was the most

common route of transmission with heterosexual transmission the most common means of transmission to women; 82% of cases have been in adult and adolescent men, and18% have been in adult and adolescent women. The numbers for 2000 show an interesting gender trend in the epidemic: cases in adult and adolescent men accounted for only 74% while cases in adult and adolescent women had risen to 25% (CDC, 2001c).

Once HIV infection is established in a human, replication proceeds rapidly. HIV is an RNA virus or a retrovirus, so called because of the "backward" manner (going from RNA to DNA) of replication. Like all viruses, HIV cannot replicate unless it is inside a living cell. HIV enters cells when the gp120 "knobs" (Figure 1) on the viral envelope bind to specific CD4 receptor sites on the cell's surface, allowing viral genetic material to enter the cell (Libman & Makadon, 2000). In the cell, viral RNA is transcribed into a single strand of viral DNA with the assistance of reverse transcriptase, an enzyme made by HIV. This strand copies itself, becoming double stranded viral DNA. At this point, viral DNA can enter the cell's nucleus and, using an enzyme called integrase, splice itself into the genome, becoming a permanent part of the cell's genetic structure. This sets the stage for two major processes: (1) during cell division, HIV DNA is replicated along with the rest of the cell's DNA and all daughter cells will be infected; and (2) viral DNA in the genome can direct the cell to make more HIV. The next stage of HIV replication is the production of long strands of HIV RNA that must be cut into appropriate lengths with the assistance of the enzyme protease. Viral RNA is then assembled and buds out from the cell, taking a bit of the cell's membrane to form a new viral envelope (Zwolski, 2001).

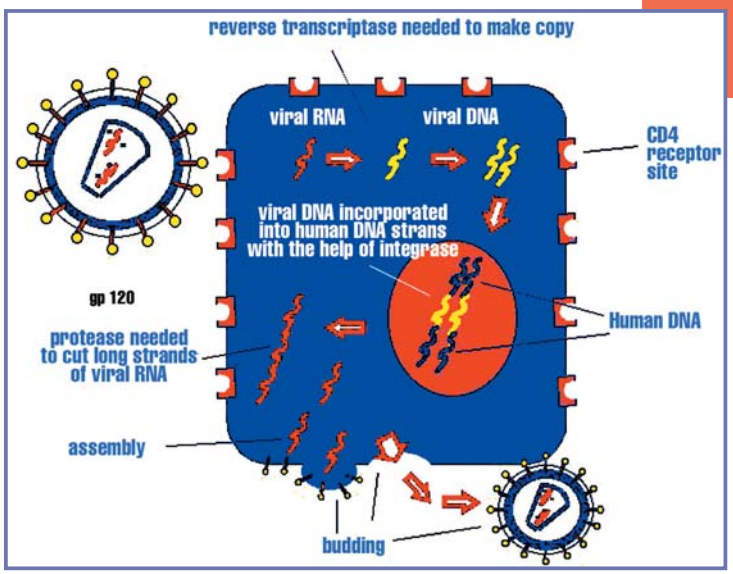


Figure 1. Intracellular Replication of HIV

HIV can infect any human cell with CD4 receptor sites. The cells most commonly infected and destroyed are those with the most CD4 receptors. These are known as T-helper lymphocytes or CD4+ T lymphocytes. CD4+ T lymphocytes are critically important in the mediation of the body's immune

response to infections and neoplasms. Loss of enough CD4 + T lymphocytes leads to immune deficiency and the opportunistic diseases associated with advanced disease. The presence of virus in the blood (viral load) fluctuates predictably during the course of untreated HIV infection. Figure 2 shows how CD4 + T cell counts, viral loads, and HIV-specific antibodies interact as HIV progresses.

Without treatment, HIV-infected patients will progress through the following stages (Figure 3):

Acute Retroviral Syndrome. Two-to-six weeks following initial infection with HIV, many patients (> 50%) develop an acute flu-like syndrome that may last 10-14 days. Clinical manifestations may include a syndrome of fever, generalized lymphadenopathy, pharyngitis, headache, myalgia, and arthralgia (Libman & Makadon, 2000). The severity of the initial acute infection with HIV is predictive of the course the infection will follow. During this stage, high levels of viral particles can be detected in the plasma, the CD4 + T cell count declines (Crandall, 1999), and seroconversion occurs. Most infected individuals will seroconvert (develop detectable antibodies) within 3 weeks to 3 months.

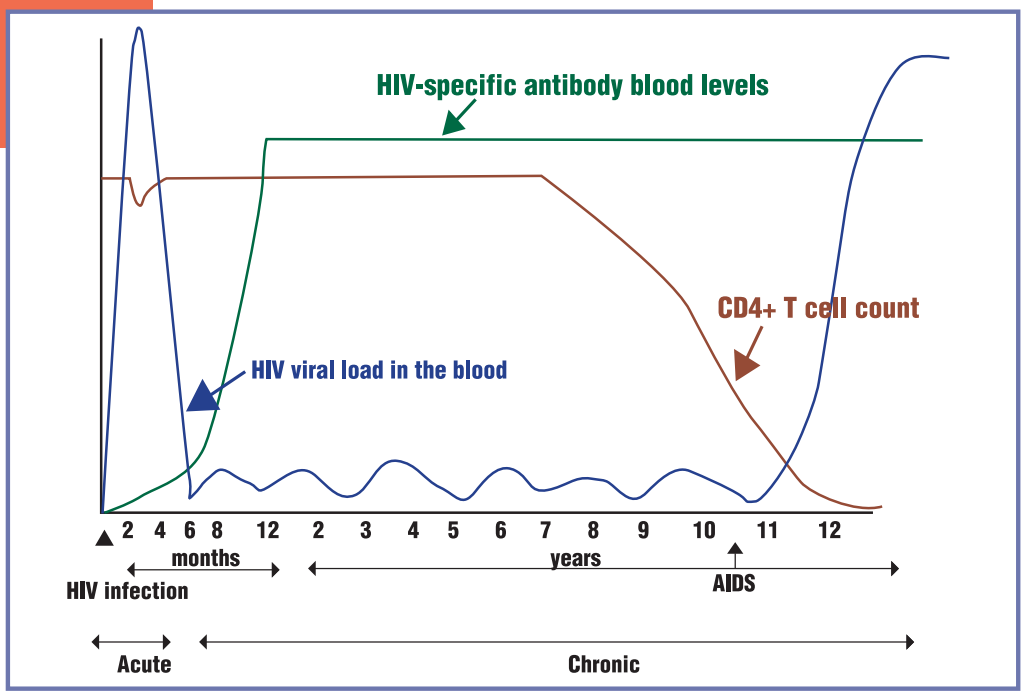


Figure 2. Lab values over the spectrum of HIV infection

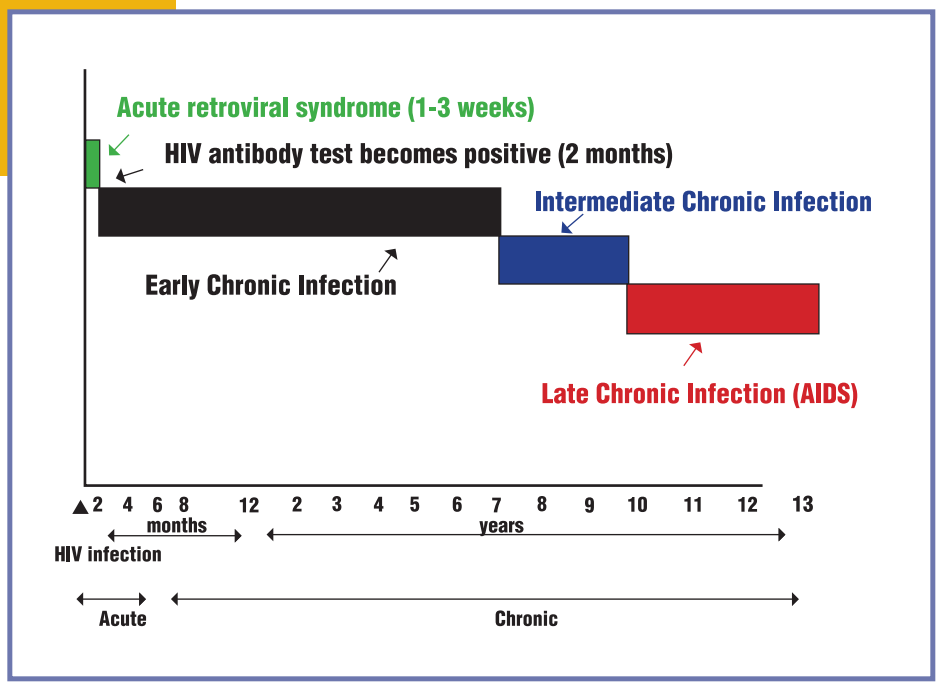


Figure 3. Timeline for the spectrum of untreated HIV disease

Early Chronic Infection. During this lengthy phase (which may last for a decade or more) patients often feel and look healthy. Their CD4 + T cell counts will be normal or slightly decreased and their viral loads will be low. Although this used to be called the asymptomatic phase, many patients will complain of intermittent fatigue, headaches, night sweats, low grade fevers, enlarged lymph nodes, weight loss, oral candidiasis, malaise, and diarrhea.

Intermediate Chronic Infection. The intermediate phase signals progression of HIV disease. CD4 + T cell counts begin to decrease as the viral load increases. Patients will experience a variety of new infections, especially those that affect the mouth, and symptoms such as those seen in early chronic infection will become more persistent.

Late Chronic Infection (AIDS). This stage is heralded by the appearance of symptoms of opportunistic diseases and specific conditions as outlined by the CDC (Table 1). Additional laboratory analysis will reveal increasing viral loads and some patients will have changes in liver functions. Patients with AIDS often have generalized lymphadenopathy, severe weight loss, fatigue, chronic diarrhea, chronic fever, and drenching night sweats, but can also have no obvious symptoms (Crandall, 1999).

Worldwide data indicate that approximately 90% of individuals with untreated AIDS die from opportunistic infections within three years of the diagnosis. The marked reduction of CD4 + T lymphocytes, to a great degree, explains the lack of immune response seen in HIV-infected patients and is

Table 1. Diagnostic Criteria for AIDS

AIDS is diagnosed when an individual with HIV develops at least one of these conditions:

1. CD4 + T cell count drops below 200 cells/mm^3.
2. Development of one of the following opportunistic infections (OIs):
   - Fungal: candidiasis of bronchi, trachea, lungs, or esophagus; *Pneumocystis carinii* pneumonia (PCP); disseminated or extrapulmonary histoplasmosis
   - Viral: cytomegalovirus (CMV) disease other than liver, spleen, or nodes; CMV retinitis (with loss of vision); herpes simplex with chronic ulcer(s) or bronchitis, pneumonitis, or esophagitis; progressive multifocal leukoencephalopathy (PML); extrapulmonary cryptococcosis
   - Protozoal: disseminated or extrapulmonary coccidioidomycosis, toxoplasmosis of the brain, chronic intestinal isosporiasis; chronic intestinal cryptosporidiosis
   - Bacterial: *Mycobacterium tuberculosis* (any site); any disseminated or extrapulmonary mycobacterium, including *M. avium* complex or *M. kansasii*; recurrent pneumonia; recurrent Salmonella septicemia
3. Development of one of the following opportunistic cancers:
   - Invasive cervical cancer, Kaposi's sarcoma (KS), Burkitt's lymphoma, immunoblastic lymphoma, primary lymphoma of the brain, or cervical carcinoma
4. Wasting syndrome occurs: defined as a loss of 10% or more of ideal body mass.
5. Dementia develops.

Modified from Centers for Disease Control and Prevention (CDC): Recommendations and Reports: 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults, MMWR, 41 (RR-17):1, 1992.

most likely related to the increase in malignant disease associated with AIDS (CDC, 1991).

Although all patients with HIV infection require excellent oral care including routine assessment and prophylaxis, individuals in intermediate and late chronic disease are more likely to present for care and to have more difficult oral pathology.

Reducing the Potential for Disease Transmission in the Dental Office

A major concern for any clinician treating HIV-infected patients is to minimize the risk of exposure for themselves, their staff, and other patients. Dental procedures frequently cause bleeding and exposure to infected blood is a known means of HIV transmission. Saliva has not been shown to transmit HIV in a dental setting, but the potential for exposure to bloody saliva does exist. To reduce the risk of disease transmission, the American Dental Association (ADA), the Occupational Safety and Health Association (OSHA), and the CDC have set standards of infection control for dental health care personnel (DHCP). The following summary highlights regulations based on CDC recommendations. For complete, in-depth coverage on use and care

of sharp instruments and needles, sterilization, disinfection, handling of biopsy specimens, and disposing of waste materials, please refer to the CDC (Abel et al., 2000; CDC, 1993).

Infectious organisms can be spread through several routes in the dental office: direct skin or percutaneous exposure to blood, oral fluids, or other secretions; indirect contact with contaminated instruments, operatory equipment or environmental surfaces; and/or contact with airborne contaminants present in either droplet spatter or aerosols of oral and respiratory fluids. Infection via any of these routes requires that all of the following conditions be present (commonly referred to as "the chain of infection"): a susceptible host; a pathogen with sufficient infectivity and numbers to cause infection; and a portal through which the pathogen may enter the host. Effective infection control strategies are intended to break one or more of these "links" in the chain, thereby preventing infection. HIV can be transmitted through sharps injuries or direct contact with open wounds on the skin or mucous membranes. There is no evidence that HIV is transmitted via the airborne route or insect vectors.

DHCP are at a *slightly* increased risk of exposure to HIV and other blood borne organisms. This risk can be reduced through the use of precautions.

Because individuals with an infectious disease cannot always be identified through history review or physical examination, the CDC recommends that DHCP follow a standard set of precautions for all patients at all times. The use of these precautions has reduced the chance that an infection can be transmitted in the dental operatory. Standard precaution procedures are widely publicized and describe techniques used to reduce contact with organisms (breaking the chain at the portal of entry) and the potential transmission of infectious agents. These precautions protect DHCP from all bloodborne organisms, including HIV.

DHCP must wear protective devices designed to protect personnel and patients in dental-care settings. Medical gloves (latex or vinyl) must be worn when there is any potential for coming into contact with blood, blood-contaminated saliva, or mucous membranes. Nonsterile gloves are appropriate for examinations and other non-surgical procedures; sterile gloves should be used for surgical procedures. Before treatment of each

patient, DHCP should wash their hands and put on new gloves; after treatment or before leaving the dental operatory, DHCP should remove and discard gloves, then wash their hands. DHCP always should wash their hands and reglove between patients.

Chin length plastic face shields or surgical masks and protective eyewear should be worn when splashing or spattering of blood or other body fluids is likely, as is common in dentistry. Masks should be changed between patients or when wet or soiled. Eyewear should be washed with an appropriate cleaning agent and, when visibly soiled, disinfected between patients.

Protective clothing (reusable or disposable gowns, laboratory coats, or uniforms) should be worn when clothing is likely to be soiled with blood or other body fluids. Reusable protective clothing should be washed, using a normal laundry cycle, according to the instructions of detergent and machine manufacturers. Protective clothing should be changed at least daily or as soon as it becomes visibly soiled.

Impervious-backed paper, aluminum foil, or plastic covers should be used to protect items and surfaces (e.g., light handles or x-ray unit heads) that may become contaminated by blood or saliva during use and that are difficult or impossible to clean and disinfect. These coverings should be discarded and replaced between patients.

These precautions significantly reduce the risk of exposure to HIV when used consistently and correctly. Unfortunately, humans are not perfect and accidents can happen. Should a blood exposure occur, the CDC has developed guidelines for post-exposure prophylaxis (PEP). These guidelines, summarized in the attached PEP Guide, cover HIV, HBV, and HCV.

Implications for Oral Health Care Providers

Oral manifestations of HIV are common (Table 2) and may be the first clinical features of the disease noted by the patient and/or health care provider (Greenspan & Greenspan, 1997). Because the DHCP may be the first to recognize the signs and symptoms of HIV, each provider must be adept at taking a medical/dental history, examining the oral cavity and surrounding tissues for signs of disease, and recognizing when an abnormality is present. Effective treatment plans cannot be developed without a definitive diagnosis for the abnormalities discovered. Proper diagnosis and treatment have been shown to reduce the morbidity associated with HIV infection and to increase the life span of the infected individual. Providers reviewing this module will learn about a variety of oral lesions, some of which also occur in patients without HIV infection (Abel et al., 2000).

TABLE 2. ORAL MANIFESTATIONS OF HIV INFECTION

Fungal Infections	Candidiasis* Pseudomembranous Erythematous Hyperplastic Angular chelitis	Histoplasmosis Cryptococcosis Geotrichosis
Bacterial Infections	Linear gingival erythema* Necrotizing ulcerative periodontitis* Necrotizing stomatitis	*Mycobacterium avium* intracellulare Actinomycosis
Viral Infections	Herpes simplex* Herpes zoster (varicella zoster) Cytomegalovirus Epstein-Barr virus Hairy leukoplakia	Human papillomavirus Oral warts Condyloma acuminatum Focal epithelial hyperplasia
Neoplasms	Kaposi's sarcoma* Non-Hodgkin's lymphoma	
Others	Facial palsy Trigeminal neuropathy Recurrent thrombocytopenic purpura Recurrent aphthous ulceration* Major Minor Herpetiform	Immune thrombocytopenic purpura Salivary gland enlargement Xerostomia Melanotic pigmentation

**More common oral lesions*

Adapted from: Little, J.W., Falace, D. A., Miller, C.S., & Rhodus, N.L. (2002), Dental management of the medically compromised patient, 6th ed. St. Louis, MO: Mosby.

Dental practitioners should understand the relevance of the comprehensive dental exam in relation to the detection of HIV infection (Cruz et al., 1996). A thorough head and neck examination must be performed. Any pathologic conditions that are found should be evaluated comprehensively and not in isolation from other oral health problems. A proper dental examination is of critical importance because many physicians do not perform thorough intraoral examinations at routine visits. It is the responsibility of the dental practitioner to screen for oral cancer and intra-oral lesions that may be indicative of HIV, oral disease, or oral/perioral signs of other systemic diseases. Although it is not the purpose of this module to completely describe the head, neck, and oral examination, all patients should have a thorough examination of these areas at every appointment.

CASE #1

Subjective information: Belinda, a 26-year-old Caucasian female, presents to your dental office and says, "I want my teeth fixed before I get married in eight weeks." The patient, originally from the area, had been living out of state for a few years and has recently returned to live with her fiance. Upon reviewing the patient's history, you encounter the following:

Drug History: Belinda denies use of alcohol, tobacco, or drugs. She presently takes birth control pills and an occasional over-the-counter allergy medication. She has no known drug allergies.

Medical History: The patient's medical history is unremarkable except that she reports having "bad flu" several times over the past year. Her physician prescribed antibiotics and she states, "I got better." She has had no surgery or hospitalization.

Dental History: Belinda reports that she has not seen a dentist in at least two years. She states that her two lower front teeth had become very loose so she pulled them out because "they seemed like they were going to fall out." She further says, "I want to have a pretty smile when I get married."

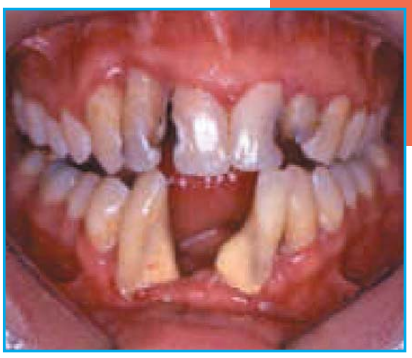
Social History: Belinda lived with an injection drug user for two years when she was in her late teens. She did not use drugs herself, but had a sexual relationship with the man.

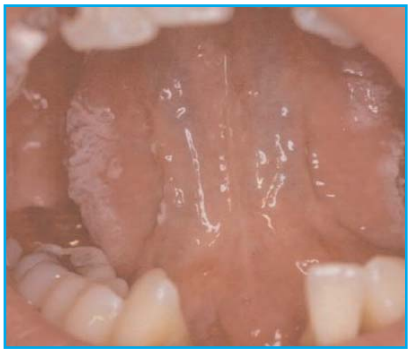
Assessment: As a dental practitioner, you consider Belinda's risk for HIV based on her current and past sexual activities. Her use of birth control pills may indicate that she does not use condoms, but you would need to ask this question specifically. She has also complained of severe flu symptoms that may indicate seroconversion illness or intermittent symptoms of early chronic HIV infection. She needs a complete and thorough comprehensive dental examination including both hard and soft tissues.

Examine the patient's head, face, neck, and hands/fingers for lesions and abnormalities because many diseases and conditions can exhibit signs in these areas. Palpate the patient's temporomandibular joint and facial musculature. Also palpate the patient's lymph nodes beginning in the submandibular area extending down the cervical chain along the sternocleidomastoid muscle into the clavicular area for any swellings or abnormalities.

Once this portion of the exam is complete, proceed intra-orally. Examine the commissures of the lips as well as the lips themselves. Check the palate, buccal mucosa, gingiva, and sublingual area for leukoplakia, erythroplakia, ulcerations, or any other abnormalities. Examine the tongue – dorsal, ventral, and the lateral borders, especially the posterior lateral borders. The posterior lateral borders can be difficult to assess, but an effective method to check this area is to use a 2x2 gauze to grasp the tip of the patient's tongue and carefully pull it to one side, then the other. Following this, examine the soft palate, pillar and trigone area, and retropharyngeal area. Finally, examine the patient's dentition and periodontal structures. A full mouth series of radiographs and periodontal probing is also essential during each new patient exam (Abel et al., 2000).

Objective findings: The comprehensive clinical exam on Belinda reveals advanced, generalized periodontal disease with premature loss of several permanent teeth. Leukoplakic patches are seen on the lateral borders of the tongue. Erythematous, papillary patches are also seen on the soft palate. Her dry mouth indicates decreased salivary flow. Another significant finding is generalized gross decay that harbors multiple microorganisms (including candida) contributing to oral disease.





Assessment: What are the differences between gingivitis associated with HIV infection and gingivitis found in the non-HIV infected patient?

The presentation of linear gingival erythema (LGE) can be one of the early signs of HIV infection. Until a few years ago, this condition was called HIV-gingivitis (HIV-G). LGE has a distinct clinical appearance that can greatly

assist the clinician in developing a differential diagnosis. The initial feature of LGE is a distinctive red line (1-3mm wide) at the free gingival margin with or without punctate erythema of the alveolar gingiva. The patient may encounter pain, spontaneous bleeding, or bleeding when brushing, flossing, or eating. It is possible that the erythematous component is due to concomitant oral candidiasis. LGE differs from gingivitis in the patient without HIV in that ordinary gingivitis is seen with poor oral hygiene, whereas LGE can be seen even with excellent oral hygiene and little or no plaque accumulation. Within 10-20 days of plaque accumulation, clinical signs of gingivitis are established in most individuals, although this varies greatly, with some individuals being intrinsically resistant and others more prone to overt gingivitis. Therefore, gingival lesions as those described for LGE, in the absence of local irritants, that do not respond to conventional periodontal therapy can be suggestive of HIV infection. Without treatment, gingivitis may progress to a destructive periodontitis; this progress may take place within weeks. Treatment includes intensive daily oral hygiene, scaling and root planing (if necessary) with 10% betadine irrigation, Peridex (chlorhexidine gluconate 0.12%) home rinses, and careful follow-up and maintenance.

Rx: Peridex (chlorhexidine gluconate 0.12%)
Disp: Three 16 oz bottles
Sig: Rinse with ½ oz for 30 sec., 2x/day after oral hygiene for 2 weeks

Periodontal disease in HIV-infected patients has many of the same clinical presentations as those seen in immune competent patients. However, periodontitis in the presence of HIV tends to be more severe, progresses more rapidly, and is often much more painful than periodontitis in a non-HIV infected person. As seen in the more common forms of periodontitis, HIV-associated periodontal (HIV-P) disease exhibits destruction of the periodontal attachment and local necrosis of the tissue. In contrast to periodontitis in the immune competent individual, HIV-P is also sometimes referred to as necrotizing ulcerative periodontitis (NUG) (HIVdent, 2001).

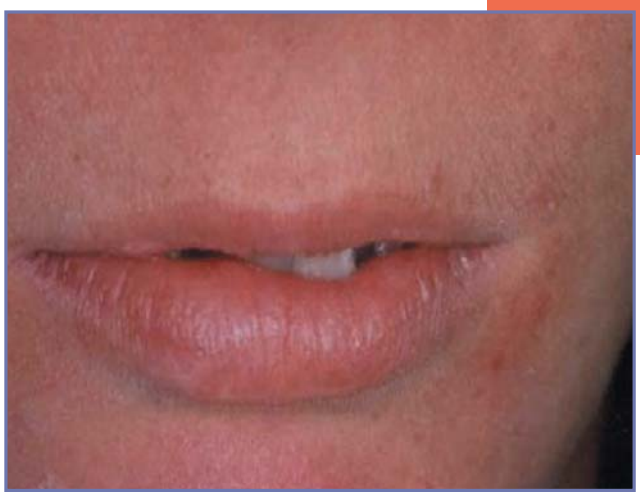
Treatment for periodontitis begins with patient education regarding causative factors and preventive measures. For HIV-P, gross debridement is often initiated with 10% betadine irrigation. The patient is re-evaluated one week later (or sooner if necessary) and then scaling and root planning in all four quadrants is scheduled. Careful follow-up and maintenance is crucial. Recall appointments should be scheduled every four weeks until stable, and then recall appointments at two to three month intervals. Advanced, non-

responsive cases may require more frequent treatment. Because there is no evidence to suggest that HIV is spread through aerosols, ultrasonic irrigation may be used in the dental operatory. Whenever possible, high-speed evacuation should be used during ultrasonic cleaning procedures.

Since antibiotics are frequently necessary to control infection, suggested prescriptions include:

Rx: Metronidazole 250 mg
Disp: 28-40 tabs
Sig: Take 1 tab 4x/day for 7-10 days
-OR-
Rx: Augmentin 500 mg
Disp: 28-40 tabs
Sig: Take 1 tab 4x/day for 7-10 days
-AND-
Rx: Peridex (chlorhexidine gluconate 0.12%)
Disp: Three 16 oz bottles
Sig: Rinse with ½ oz for 30 sec., bid after oral hygiene

Objective findings: On clinical examination, you also find a slight crusting bilaterally at the commissures of Belinda's mouth.



Assessment: Taken in context with the other findings, what is the most likely diagnosis?

The most likely entity causing these signs is angular cheilitis. Fungal infections, including angular cheilitis, are common findings in HIV-infected individuals. Angular cheilitis, though prevalent in HIV-infected individuals, is also seen in individuals who do not have HIV infection. It is classified as one of three common types of candidiasis seen in HIV along with erythematous (atrophic) candidiasis, arguably the most under diagnosed oral disease seen in people living with HIV infection (Reznik, 1999), and pseudomembranous candidiasis. Candidiasis is more common in HIV-infected women (Campisi, Pizzo, Mancuso, & Margiotta, 2001) and in current smokers who have HIV (Palacio,

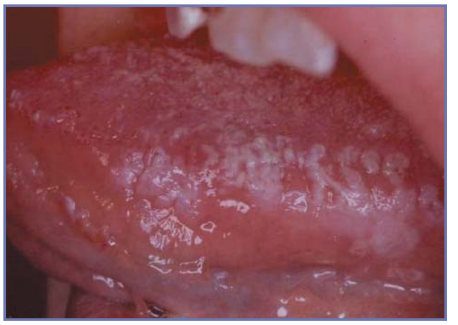
Hilton, Canchola, & Greenspan, 1997). Angular cheilitis often appears as a cracked or fissured area radiating from the corner of the mouth, often associated with white, yellow or tan crusts and scales. Since angular cheilitis is a fungal condition, it can be treated effectively with topical antifungal creams or ointments. Combining antifungal cream with a mild steroid (triamcinolone or betamethasone) can speed healing of the skin/mucosal fissures. However, the prescriber should be aware that steroids should not be applied to viral lesions without concomitant anti-viral therapy (Greenspan & Greenspan, 2001).

Patients with angular cheilitis will invariably have an associated oral fungal infection. Although treatment for angular cheilitis also involves treatment of intraoral candidiasis, effective topical antifungal treatment at the corners of the mouth can include these medications:

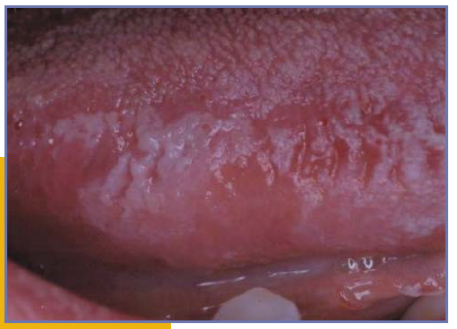
Rx: Nystatin ointment or Mycelex (Clotrimazole 1%) ointment, Lotrisone (0.05% betamethasone plus 1% Clotrimazole), or ketoconazole cream (2%)
Disp: 15g
Sig: Apply sparingly to affected areas q2h during waking hours

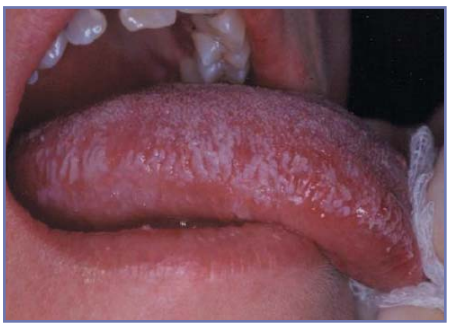
Moderate to severe candidiasis may require systemic therapies such as ketoconazole, itraconazole, or fluconazole. As with topical antifungal therapy, treatment should last two weeks (Reznik, 1999).

Objective Findings: The following lesions are found bilaterally on Belinda's dorsolateral tongue borders. The lesions demonstrate a corrugated appearance, do not have a red component and cannot be rubbed off with gauze.



Assessment: What is the most likely diagnosis?





Based on the history and physical examination, the differential diagnosis for these patches includes hairy leukoplakia (HL), candidiasis (or other fungal infection), and (frictional) hyperkeratosis, lichen planus, and epithelia dysplasia. Taken in context with the other visible lesions, the most likely entity is HL. With HIV infection, HL often initially manifests as a discrete, shaggy white patch on the lateral borders of the tongue. Because Epstein-Barr virus (EBV) particles are seen in electron microscopic examination, it is thought that HL is a result of concomitant HIV and EBV infection. HL can also manifest with one or more of the following textures: corrugated, smooth, flat, papular, or "hairy" appearance. HL cannot be wiped off which differentiates it from a lesion like pseudomembranous candidiasis that can be wiped off leaving a red and sometimes bleeding surface. HL may appear unilaterally or bilaterally; bilateral presentation is the most common. Although HL most often presents on the lateral borders of the tongue, in advanced HIV infection it can be seen on the buccal mucosa, labial mucosa, floor of mouth, soft palate, and oropharyngeal mucosa. HP is usually asymptomatic, but the lesion may cause discomfort and, especially when super-infected with candida, present a cosmetic problem.

Diagnosis of HL is extremely important and remains a good predictor of HIV disease progression. It must be remembered, however, that the lesion can occasionally be found in persons not infected with HIV.

No definitive treatment has been identified and HL is often left untreated. Combination antiretroviral therapy (ART), along with any one of several antiviral drugs, including acyclovir, has been shown to reduce the size of HL lesions. Antifungal therapy is appropriate as candidiasis is often found to be associated with the lesion (Greenspan & Greenspan, 2001). More importantly, oropharyngeal candidiasis is extremely common, eventually affecting over 90% of people with a diagnosis of AIDS (Libman & Makadon, 2000).

Assessment: Your exam strengthens suspicions of HIV infection. A medical referral is appropriate. What tests will help to determine Belinda's HIV status?

Testing for HIV Infection

A variety of antibody tests are used to screen for HIV infection. Table 3 describes the screening process that must be accompanied by pre- and post-test counseling. Tests are available from primary care clinicians, health care plans, and most local health departments. When a patient has limited options for health care or is fearful of being tested by her physician, the health department is a good referral.

Rapid tests. Rapid HIV screening tests, first approved in 1996, can be performed in an average of 10 minutes. In terms of time and convenience, these tests offer dramatic improvements over standard antibody tests that require days or even weeks for results. Most significantly, individuals with negative test results do not have to return for a second visit to obtain their test results; they receive them shortly after the test is performed. For positive tests, however, a confirmatory EIA and Western blot protocol is still required to eliminate false positives. This requires a time delay and a second visit or appointment to obtain the results (Keenan & Keenan, 2001).

Rapid test methodologies include "dot blot" or "immunoblot" assays that produce a colored dot on the solid phase surface, with or without an anti-human immunoglobulin control. Dipstick assays are also available. The Murex Single-Use Diagnostic System (SUDS®) for HIV is the only rapid test currently approved for use in the United States (Bartlett & Gallant, 2001).

Table 3. HIV Antibody Test Screening Process

The following steps are used in the process of testing blood for antibodies to HIV:

1. A highly sensitive enzyme immunoassay (EIA, ELISA) is done to detect serum antibodies that bind to HIV antigens on test plates. Blood samples that are negative on this test are reported as negative.
2. If the blood is EIA reactive, the test is repeated.
3. If the blood is repeatedly EIA reactive, a more specific confirming test, such as the Western blot (WB) or immunofluorescence assay (IFA), is done.
   - WB testing uses purified HIV antigens electrophoresed on gels. These are incubated with serum samples. If antibody in the serum is present, it can be detected. The CDC and the Association of State and Territorial Public Health Laboratory Directors define a positive Western blot assay as any two of three bands (p24, gp41, gp120/160) that correspond to HIV markers present in the specimen. The criteria for a negative Western blot interpretation specify the total absence of bands. All other band patterns are regarded as indeterminate, i.e., bands are present but they do not fulfill diagnostic criteria.
   - IFA is used to identify HIV in infected cells. Blood is treated with a fluorescent antibody against p17 or p24 antigen and then examined using a fluorescent microscope.
4. Blood that is reactive in all of the first three steps is reported as HIV-antibody positive. The combination of EIA and Western blot assay has an extremely high positive predictive value (persons with positive tests are very likely to be infected), even in low-risk populations.
5. If the results are indeterminant, the following steps need to be taken:
   - If in-depth risk assessment reveals that the individual does not have a history of high risk activities: reassure the client that s/he is extremely unlikely to be infected with HIV and suggest re-testing in 3 months.
   - If in-depth risk assessment reveals that the individual does have a history of high risk activities: repeat antibody test at 1, 2, and 6 months; discuss harm reduction measures to protect partners from infection; consider tests for HIV antigen detection.

The results of a number of studies confirm that the accuracy of rapid tests is similar to standard ELISA screening protocols. Rapid tests are simple to perform and can be used in a wide variety of settings. Because of this, they are likely to be used with increasing frequency in many settings, including emergency rooms, indigent clinics, "point of care" testing, and in testing situations where time is critical (Keenan & Keenan, 2001).

When can HIV antibodies be detected? The "window period" is a critical concept in HIV testing. The window period is the time between initial infection with HIV and the development of enough antibodies to be detected through testing. In general, 3 to 12 weeks is required after infection (Libman & Makadon, 2000). A recently infected individual, therefore, may not test positive for HIV but could still transmit HIV to others. The virus is not latent during the window period or any subsequent period. In fact, the viral load is higher after initial infection than any period until advanced HIV disease (Figure 1). After this initial "spike," the viral load decreases to a more stable "set point." Understanding the window period is important for recommendations regarding further testing and for risk prevention. A recently exposed person should be advised to return for HIV antibody testing 6 weeks and 3 months after the exposure incident. Persons concerned about risk or potential exposure should be counseled to take precautions to prevent transmission of HIV during the window period. It is important to ensure that persons receiving pre- and post-HIV test counseling understand the window period concept (Bartlett & Gallant, 2001).

Test Counseling

Pre test counseling. People who are identified as being at risk for HIV should receive pretest counseling and be encouraged to be tested. Pretest counseling guidelines are available from a variety of sources. Basically, pretest counseling consists of a process starting with a risk history and an explanation of prevention measures. Information about the test, including an explanation about what the test can and cannot determine is also necessary. Most states require informed consent prior to testing because of the emotional, physical, and social implications of having a diagnosis of HIV infection. HIV infection is a reportable disease in most states and AIDS is reportable in all states (CDC, 2001d).

Post-test counseling. Post-test counseling should be performed with all patients who return for test results. Counseling sessions should be adapted for each patient according to individual variables including the result of the test, patient response to the test result, and the emotional vulnerabilities and needs of the patient. Seronegative post-test counseling should:

- Reinforce and review risk elimination/risk reduction guidelines for the prevention of HIV transmission.
- Confirm that the last possible exposure was not within the last six months. If it was, encourage retesting 6 weeks to 3 months after the most recent exposure.
- Provide information on community support services, drug treatment programs, and behavior modification services, as needed.
- Provide information on psychosocial support, if appropriate.

In the case of positive test results, components of post-test counseling may be divided among two or more visits to address different issues. It is important that each patient be counseled according to his/her own needs and responses. Seropositive post-test counseling should:

- Assess the individual for mental distress. Assess availability of personal support systems (friends, family, etc.). Provide information on additional counseling and support services in the community.
- Review guidelines for eliminating or reducing the risk of transmission to others.
- Discuss the terminology of HIV and AIDS, concepts like CD4 cell and viral load, and the signs and symptoms of HIV-related illness.
- Discuss the importance of avoiding additional infections that will stress the immune system, such as sexually transmitted diseases, colds, flu, and other infections.
- Encourage medical follow-up in order to obtain a baseline physical examination, to have appropriate lab tests (including PPD skin test for TB and pregnancy test, if indicated), and to be evaluated for drug therapy and prophylaxis.
- Review basic principles of good health such as nutrition, stress reduction, sleep and exercise, and good dental care.
- Discuss plan for partner notification.
- Provide educational materials, as appropriate.
- Assess the need for a case manager or care coordinator. Assistance with medical and social needs is very important (CDC, 2001d).

Disclosure in health care settings. Disclosure of HIV infection to others is a serious and sensitive issue. Informed consent must be obtained for any disclosure to other service providers, and health care providers have legal and ethical responsibilities to maintain the confidentiality of patient status and treatment. This can be especially challenging in small communities or rural areas where confidentiality can be breached without even mentioning a name. Despite this, patients should be encouraged to disclose a diagnosis of HIV infection to all health care personnel so that appropriate treatments can be provided. Although this makes logical sense, patients will not disclose if

they do not feel safe. It is essential that all providers, including office staff, be oriented to the responsibility of maintaining confidentiality and managing clinic records appropriately.

Assessment: Belinda is found to be HIV infected. Her CD4 + T cell count is 250 cells/mm^3 and her viral load is 52,000 copies/mm^3. Her physician orders antiretroviral therapy (ART) with Combivir (zidovudine + lamivudine) and indinavir (Crixivan) and refers her back to you for dental care.

What do you need to know about antiretroviral agents?

Despite nearly 20 years of ongoing research by some of the world's finest scientists, there is no cure for HIV infection. Ongoing research and clinical trials have, nevertheless, lead to effective treatments to reduce the progression of HIV infection. Highly active ART has been shown to reduce the opportunistic infections (OIs), viral load, and progress of some malignancies associated with advanced HIV infection. This is especially true with oral conditions; patients on highly active ART had a significantly lower prevalence of all oral lesions (Patton et al., 2000). One study demonstrated better than 30% decreases in oral candidiasis, herpes simplex, Kaposi's sarcoma, and periodontal disease (Ceballos-Salobrena, Gaitan-Cepeda, Ceballos-Garcia, & Lezama-Del Valle, 2000). The goals of drug therapy in HIV infection are to:

- decrease HIV RNA levels to < 5000 copies/mm^3 (undetectable HIV RNA levels are possible and preferred),
- maintain or raise CD4 + T cell counts to > 500 cells/mm^3 (a range of 800 to 1200 cells/mm^3 is preferred), and
- delay the development of HIV-related symptoms, including a wide range of opportunistic diseases.

Although treatment with antiretroviral regimens has vastly improved life for many patients, it is not an easy solution, especially since patients should expect to be on these drugs for the rest of their lives. ART often requires complex dosing schedules, there can be major side effects, and a potential for serious consequences exists if viral resistance develops. Resistance occurs rapidly when patients miss drug doses (better than 90% adherence is needed to prevent resistance) or when inadequate ART is prescribed. Clinicians who work with patients on ART need a thorough understanding of the medications and their actions, side effects, potential drug interactions, and contraindications. Consultation with the patient's physician is normally indicated to assess lab values and to make decisions about prescriptions for dental problems.

Because of the rapidity with which new therapies are evolving and the desire to delay side effects and resistance, there has been considerable discussion about how and when to initiate therapy. Government recommendations for starting therapy in the chronically infected patient are summarized in Table 4 (CDC, 2001b).

Currently approved drugs fall into four groups that inhibit the ability of HIV to replicate. Nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), and nucleotide reverse transcriptase

Table 4. Indications for the Initiation of Antiretroviral Therapy in the Chronically HIV-Infected Patient

Clinical Category	CD4+ T Cell Count	Plasma HIV RNA	Recommendation
Symptomatic (AIDS, severe symptoms)	Any value	Any value	Treat
Asymptomatic, AIDS	CD4+ T cells $< 200/mm^3$	Any value	Treat
Asymptomatic	CD4+ T cells $200/mm^3$–$350/mm^3$	Any value	Treatment should generally be offered, though controversy exists*
Asymptomatic	CD4+ T cells $< 350/mm^3$	> 30,000 (bDNA) or > 55,000 (RT-PCR)	Some experts would recommend initiating therapy, recognizing that the 3-year risk of developing AIDS in untreated patients is > 30%. In the absence of very high levels of plasma HIV RNA, some would defer therapy and monitor the CD4+ T cell count and level of plasma HIV RNA more frequently. Clinical outcomes data after initiating therapy are lacking.
Asymptomatic	CD4+ T cells $< 350/mm^3$	< 30,000 (bDNA) or < 55,000 (RT-PCR)	Many experts would defer therapy and observe, recognizing that the 3-year risk of developing AIDS in untreated patients is < 15%.

Revised from *Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents*, Department of Health and Human Services (DHHS), 2001.
*Clinical benefit has been demonstrated in controlled trials only for patients with CD4+ T cells $< 200/mm^3$. However, most experts would offer therapy at a CD4+ T cell threshold $< 350/mm^3$. All decisions to initiate therapy should be based on prognosis for disease-free survival in the absence of treatment, as determined by the CD4+ T cell count and level of plasma HIV RNA, the potential risks and benefits of therapy, and the willingness of the patient to accept therapy.

inhibitors all work by inhibiting the activity of reverse transcriptase at the beginning of the replication cycle. Protease inhibitors (PIs) work by interfering with the activity of protease near the end of the replication process (Figure 1). Please refer to *A Pharmacists Guide to Antiretroviral Medications for HIV-infected Adults and Adolescents* (enclosed) for detailed information on drug-specific dosage, side effects, and drug interactions.

A Word on Oral Warts

Human papillomavirus (HPV), a cause of oral and genital warts, has been a popular topic in recent dental literature, particularly as increasing rates of oral warts have been linked to ART with PIs. Although oral warts are seen in patients without HIV infection, the incidence is more common in individuals who are immune suppressed, including those with HIV infection. There is some controversy, however, concerning whether this increase is truly linked to ART and the PIs. Most researchers agree that there is an overall decrease in other oral manifestations when ART with or without PIs is used. Researchers at the University of California, San Francisco have found that since the introduction of PIs into ART, oral warts have become a growing problem among HIV-infected patients while other common oral lesions such as candidiasis and HL are decreasing (HIVdent, 1999). Researchers at the University of Texas, Houston Health Sciences Center Dental Health Branch found that while data support increasing incidences of oral warts in HIV-infected patients, no definite correlation could be found (Felefli et al., 2000). Other researchers have shown three-fold increases in oral warts in patients on ART without a PI and six-fold increases in patients on ART with a PI (Greenspan et al., 2001). Until a definitive correlation can be shown, all that can be assumed is a link. This distinction does not change the take-home message: all patients with HIV should be assessed for oral warts as part of routine, comprehensive oral health care. Oral warts may appear as cauliflower-like, spiky, or slightly raised with a flat surface (Greenspan & Greenspan, 1997). Oral warts are most effectively removed via surgical or laser excision, but recurrence is common. Treatment may, therefore, be reserved for lesions that interfere with function or are esthetically disturbing to the patient.

Plan: What type of oral health care treatment course is indicated for Belinda?

The dental practitioner should begin treatment for oral pathology as soon as possible using information discussed in the previous sections. Medical consultation and referral should continue for as long as the patient is in the dental provider's care.

Please use the rest of this module as a workbook for the next three cases.

This symbol indicates a hidden answer. Please write your response to the question in the space provided. When you are ready to check your answer, run the tip of the enclosed pen over the space below the and the correct response will appear.

CASE #2

Subjective information: Larry is a 32-year-old African American male who has been in your care for several years. He presents today with the chief complaint of, "The roof of my mouth on one side stings like crazy. It started about two weeks ago and seems to be getting a little better in the last few days." When you review his records you come across the following:

Drug History: Larry denies use of tobacco or illegal drugs. He reports occasional use of alcohol at 2-4 beers a week depending on his social activities. He is currently not taking any medications except for multivitamins.

Medical History: Larry's medical history has been non-contributory.

Dental History: He has had regular dental treatment, but it has been about a year since you last saw him.

Social History: Larry is a college graduate who works as an engineer. He states his sexual orientation to be homosexual.

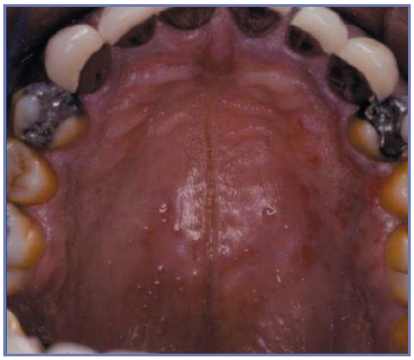
Is there anything in Larry's history that would indicate a risk of HIV infection? If so, what?

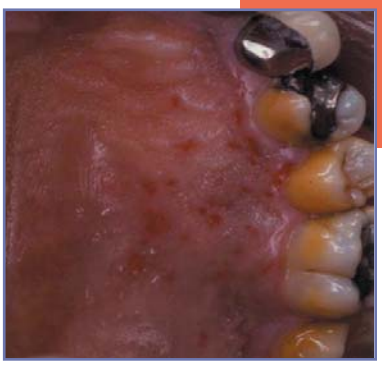
_____

_____

Larry has told you that he is homosexual. This is not enough to create a risk for infection with HIV. You will need to find out if Larry is (or has been) sexually active, whether he is predominantly the "giver" or the "receiver" of the semen, and if he uses condoms consistently and correctly. Sometimes these are difficult questions for the DHCP to ask. Please refer to STD/HIV Risk Assessment: A Quick Reference Guide *(included).*

Objective findings: Intraoral examination reveals multiple unilateral shallow ulcers (punctate) on the right side of the hard palate.





Assessment: Develop a differential diagnosis for this collection of lesions and indicate which is most likely:

_____

_____

_____

The most likely diagnosis is herpes zoster (varicella zoster virus or VZV), or shingles. VZV is also the virus that causes chicken pox.

What would help the practitioner determine that the lesion is VZV?

First and foremost, one must look at the obvious signs and symptoms that the patient reports. The patient's first complaint is pain of two weeks duration that has decreased over the past few days. Pain associated with herpes zoster oral lesions is usually quite severe. The second major observation is the unilateral appearance of the lesion.

Herpes zoster most probably is caused by reactivation of VZV lying dormant in sensory ganglia of patients whose immunity to the virus has diminished (Wormser, 1998). Herpes zoster has a tendency to increase in incidence with age. Approximately 20% of reported cases involve the trigeminal nerve. The virus produces crops of vesicles along the distribution of the nerve. Oral lesions are seen with skin lesions when the second and third divisions are affected. Intraoral herpes zoster lesions are usually

unilateral. Pain and itching are common precursors to oral lesions and patients may complain of pain in otherwise healthy teeth (referred pain). Skin lesions begin as vesicles, then rupture and crust over. Oral lesions are vesicles that rupture to form ulcers. The most frequently affected areas of the oral mucosa are the lips, tongue, hard and soft palate, and buccal mucosa. The incidence of herpes zoster is increased in patients with low general resistance, in patients receiving corticosteroids or immunosuppressive drugs, or in those with a systemic malignancy. The HIV-infected patient is more susceptible to all sorts of infections including but not limited to tuberculosis, influenza, viruses, and fungal infections. Herpes zoster will most commonly affect the mucosa. Extreme cases, however, can lead to premature exfoliation of the dentition, osteomyelitis, and extensive necrosis of the mandible with sequestration (Wormser, 1998). Treatment, which should be initiated as soon as possible, includes:

Rx: famciclovir 500mg
Disp: 21 tabs
Sig: Take 1 tab PO q8h until gone
-OR-
Rx: acyclovir 800mg
Disp: 35 tabs
Sig: Take 1 tab 5x/day until gone

What would your treatment plan include?

Plan: *It will be important to discuss your findings with Larry, including your concerns about HIV infection. A medical referral is indicated to rule out HIV. Assure him that you will continue to treat his oral health problems and that you will consult with his physician about treatment plans. Consider anti-viral therapy even though the lesions seem to be subsiding. Teach Larry about VZV and prescribe therapy to begin as soon as he experiences a future prodrome or full out break.*

CASE #3

Subjective Information: Tomas, a 27-year-old Hispanic male, presents to your dental office as a new patient. His chief complaint is, "I have a swelling on my gums that bleeds when I brush. Do you think I have cancer?" Your risk assessment reveals:

Drug History: Tomas reports a six/pack year history of tobacco use (1pack/day for six years), social alcohol use (less than 4 glasses of wine/week), and no illicit drug use.

Medical History: The medical history is non-contributory.

Dental History: He reports routine periodic dental care. His last dental visit was six months ago.

Social History: Tomas is a college graduate, single, an only child with both parents living and "healthy." He works as an investment banker.

Is there anything in Tomas' history that would indicate a risk of HIV infection? If so, what?

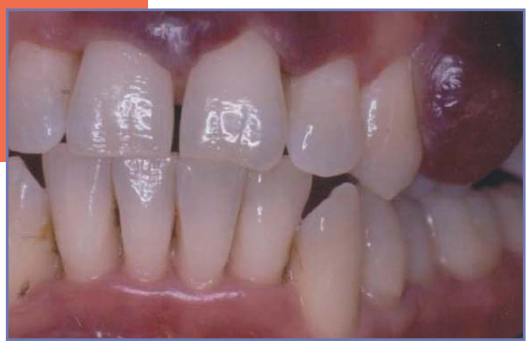
_____

_____

Tomas has not given any reason for you to suspect HIV infection. This may be because he is unaware of any risk, you didn't ask the right questions, he was not yet willing to disclose risk behaviors, or he doesn't have any risks.

Objective findings: There are two distinct findings on clinical examination. The first is an approximately 2x2 cm exophytic erythematous tumor on the facial gingiva from teeth numbers 11-12. This tumor-like lesion bleeds easily on probing. The second finding is an asymptomatic 2x1 cm purple-blue patch located on the right hard palate.

Assessment: Develop a differential diagnosis for this lesion and indicate which is most likely:



The most likely diagnosis is Kaposi's sarcoma (KS).

KS has been recognized as a medical condition, particularly in people of Mediterranean descent, since 1872. It was later seen in Central Africa as a malignant tumor and also as a complication of immunosuppressive therapy. In 1981, the first reports of KS in young men in New York City and California began to emerge (Friedman-Kien et al., 1981). Shortly after this observation, studies of homosexual men in the San Francisco area were initiated. These studies, made before the recognition of HIV as the etiologic agent for AIDS, established the palate as the most common site for intraoral KS. Although the gingiva has been identified as the second most common site for intraoral KS, it must be noted that oral KS can be found anywhere in the oral cavity.

The classic KS lesion is a vascular neoplasm found in older men of Jewish and Italian heritage. This type, found in patients without HIV infection has a 10- to 15-year survival rate in over 37% of the cases. Classic KS is usually

confined to the lower extremities. The variant associated with HIV, called "epidemic KS," is now known to be caused by the human herpes virus-8 (HHV-8), a sexually transmitted pathogen (Rohrmus, Thoma-Greber, Bogner, & Rocken, 2000)). KS is the most common AIDS-associated cancer (Feigal, Levine, & Biggar, 2000).

Intraoral KS may have a variety of clinical presentations. The early stages of KS have a reddish color, whereas older lesions tend to have a darker color. Overall, the color may range from a characteristic deep red to a bluish-purple to black. Lesions may be flat or nodular and many are asymptomatic. Nodular lesions, however, may become large or painful, and may lead to ulcerations and bleeding, interfere with speech or food intake, cause airway obstruction, or contribute to tooth loss (Feigal et al., 2000). KS is rare in children with HIV and much less common in IV drug users, women, and hemophiliacs with HIV than in homosexual men with HIV (Fischman, 1998).

What would your treatment plan include?

Plan: The important point here is recognition of these lesions. Unfortunately, not all patients will have lesions this distinct. Referral to a physician is the first step, followed with a biopsy of the lesions after medical clearance. Treatment currently consists of therapy with ART for the underlying HIV disease; some clinicians will also recommend radiation and/or chemotherapy, based on the extent of the disease. Small lesions confined to the mouth may be treated with intralesional injections of 0.2 mg/cc of vinblastine sulfate, cryotherapy, surgical excision, or radiation. Systemic therapy is reserved for patients with widespread disease or visceral involvement (Reznik, 1999; Bartlett & Gallant, 2001). Oral lesions can be especially difficult to treat with radiation and referral to a radiation oncologist is in order (Kao, Devine, & Mirza, 1999).

CASE #4

Subjective Information: Hal presents to your office as a 41-year-old male with a chief complaint of, "I've had a sore throat for 5 days and there is an especially sore spot behind my lower left molars."

Family History: Hal tells you that he has two healthy siblings. Father and mother are healthy as well.

Drug History: He reports 28-pack/year tobacco use, alcohol use (about 12 beers/week), and a history of cocaine use.

Dental History: Hal has had routine dental visits every six months for simple restorative work and prophylaxis.

Medical History: Hal reports no hospitalizations or surgery. He does say he has "not been well for several years." He says he has had many cases of the flu and that his doctor usually gives antibiotics, but that this doesn't always help.

Social History: He is divorced with joint custody of his two children. He is employed as a bartender.

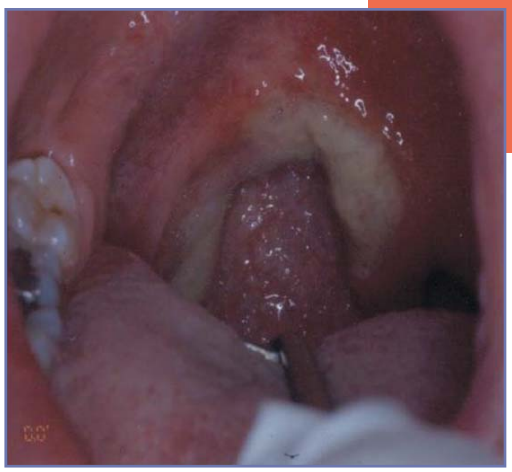
Is there anything in Hal's history that would indicate a risk of HIV infection? If so, what?

_____

_____

Hal has a history of cocaine use. At this point, you do not know how he uses the cocaine, how often he uses, if he uses with a group, or when he last used. Cocaine use in itself does not transmit HIV. If Hal shares his injection or snorting equipment with others, however, he risks exposure to the blood of his drug-sharing partners. In addition, if he had unprotected sex while under the influence of cocaine (a not unusual occurrence), he risks exposure to HIV during sexual activities. All of these issues should be addressed in a risk assessment. In addition, Hal's assessment of his health may be a further indicator of immune suppression.

Objective Findings: Bilateral lymphadenopathy was found on comprehensive examination. Hal also had enlarged submandibular nodes on the left side that were tender to palpation. Intraorally, an approximate 1x1 cm deep ulcer was located on the right oropharnyx.



Lymphadenopathy, or inflammation of the lymph nodes, is a sign of infection or simply of the body trying to fight off some type of irritant. Inflammation of the cervical or submandibular lymph nodes is often an early finding in patients with HIV but can also be seen in patients without HIV. Lymphadenopathy in these areas can also be present in conjunction with other oral diseases such as herpetic gingivostomatitis and acute necrotizing gingivitis. However, when persistent inflammation is noted in the absence of medications and infections that may precipitate enlargement, one must be suspicious. These enlarged lymph nodes are often greater than one centimeter in size and are multifocal. If any white lesions are noted during the examination, they must be managed properly. If red or purple lesions are found and cannot be explained by history (trauma-burn, chemical, physical) or proven by clinical observation (healing within 7-10 days), they must be biopsied. It is important to associate the lymphadenopathy with an oral lesion if one is present.

Assessment: Develop a differential diagnosis for these lesions and indicate which is most likely:

_____

_____

_____

_____

_____

The two most likely diagnoses are squamous cell carcinoma and aphthous ulcers.

Squamous cell carcinoma

The major oral lesion seen in this patient is representative of multiple disease processes. The reddish white appearance, or erythroleukoplakia, is similar to that of squamous cell carcinoma.

The vast majority of oral cancers in people without HIV are of epithelial origin, with most developing from tissues lining the oral cavity; hence, about 90% of oral cancers seen by dentists will be squamous cell carcinomas (National Cancer Institute, 2002). The remaining primary lesions are carcinomas arising from salivary gland tissues and lesions of other tissue types such as sarcomas and lymphomas. Squamous cell carcinoma can develop in normal-appearing tissue or, as is more often the case, in preexisting benign white or red lesions involving the oral mucosa. White lesions that cannot be scraped off and that are clinically nonspecific (leukoplakia) may be benign, pre-malignant, or malignant. Leukoplakias with areas of erythema have a three to five times greater chance of being cancerous at initial biopsy or developing into cancer than do homogenous leukoplakias, which have a 10% chance. Erythroplakia, or red lesions, in the oral cavity are of even greater concern than red-white lesions. Nonspecific red lesions are found to be malignant more often than leukoplakias and erythroleukoplakias. The erythroplakias, however, are much less common. The percentages of lesions being malignant upon initial biopsy are as follows: leukoplakia (6%), erythroleukoplakia (14%), and erythroplakia (51%) (Silverman, 1998).

Classification of Oral Carcinomas

Squamous cell carcinoma
- Carcinoma in situ
- Well differentiated
- Moderately well differentiated
- Undifferentiated

Verrucous carcinoma
Glandular epithelial tumors
Unclassified carcinoma

Regional and distant metastases are possible, but distant metastasis is rare. Regional metastasis may include local tissues and regional lymph nodes through the lymphatic system. Although rare, distant metastasis sites for squamous cell carcinoma include lung, liver, and bone. Common sites for squamous cell carcinoma intraorally include the lateral and ventral tongue, floor of the mouth, lips, and soft palate. Uncommon areas include heavily keratinized areas such as the gingiva, hard palate, and dorsum of the tongue. In general, the more anterior in the oral cavity, the better the prognosis. This is simply due to earlier detection and easier access for surgery.

Squamous cell carcinoma can be asymptomatic in early stages, often delaying detection and treatment. Squamous cell lesions may present as an exophytic mass, ulceration, a granular raised lesion, or a combination of these. Ulcerated lesions will often have raised margins that are indurated on palpation. Though often asymptomatic in early stages, more advanced

lesions may become very painful. Large lesions in the posterior portion of the oral cavity may interfere with the passage of food and air; the patient may complain of weight loss and difficulty breathing. Other complaints may include hoarseness, numbness, loosening of teeth, and change of fit for dentures. Once again, recognition of the lesions is an imperative first step (Horowitz, Drury, Goodman, & Yellowitz, 2000)

Aphthous Ulcers

Recurrent aphthous ulcerations (RAU, "canker sore," "aphthous ulcer," and "recurrent stomatitis") are characterized by recurrent ulcers of the non-keratinized oral mucosa and oropharnyx (Reznik, 1999). The most common areas of aphthous formation include the labial and buccal mucosa, tongue, and floor of the mouth. Three types of lesions are found in patients with recurrent apthous ulcers. In non-HIV infected patients, minor aphthous ulcers are the most common; in HIV-infected patients, herpetiform and major type lesions appear most often. In RAU-disposed individuals, the condition seems to be exacerbated after infection with HIV. Though aphthous ulcers can be seen in any patient, they are more prevalent in some populations: women are affected slightly more than men, and smokers less frequently than non-smokers (Palacio et al., 1997). Although the etiology or RAU is unknown, precipitating factors often include trauma, stress, and certain food products. There is usually a prodromal stage, experienced as a burning sensation, and, when the ulcer is established, pain may become intense. As one can see in the case photo, the ulcer is located on the oropharnyx and indeed appears to be very painful. One can see the typical characteristics of a major type aphthous ulcer displaying a fibrin-covered ulcerated lesion with a red halo. Topical steroids have been used to treat recurrent aphthous ulcers. Various regimens include fluocinanide 0.05% ointment mixed with equal parts Orabase applied 6x/day, or dexamethosone elixir 0.5 mg/5 ml used as a mouth rinse 2-3x/day (Greenspan & Greenspan, 1997).

What would your treatment plan include?

Plan: A medical evaluation would be pertinent in this situation, most likely with an ear, nose, and throat specialist. The lesion should be biopsied and treatment decisions would be determined by the biopsy results. Testing should also be done for HIV and other chronic, immune-suppressive conditions.

STUDY QUESTIONS

1. HIV can infect human cells with CD4 receptor sites on their cell membranes.
   a) True b) False

a) True: HIV cannot enter a cell without CD4 receptor sites. CD4 + T lymphocytes are most often infected by HIV.

2. AIDS is defined as a patient with HIV and a CD4 lymphocyte count less than 500/mm^3.
   a) True b) False

b) False: AIDS is actually defined with a CD4 lymphocyte count less than 200/mm^3 in a patient with HIV infection.

3. Which of the following has ***not*** been shown to transmit HIV:
   a) blood
   b) semen
   c) breast milk
   d) vaginal secretions
   e) saliva
   f) all of the above

e) Saliva: Blood, semen, vaginal secretions, and breast milk have all been shown to transmit HIV. Risk of transmission by direct contact with fluids other than those stated is extremely unlikely, unless those fluids are contaminated with blood. Blood and saliva are frequently mixed during dental procedures; it is the blood and not the saliva that presents a risk.

4. Transmission of infection requires all three of the following: a susceptible host, a pathogen with sufficient infectivity and numbers to cause infection, and a portal through which the pathogen may enter the host.
   a) True b) False

b) True: This is the "chain of infection."

5. List the three most consistently documented means of HIV transmission:
   1) _____
   2) _____
   3) _____

Unprotected sexual intercourse, sharing equipment to inject drugs, and perinatal transmission. HIV is primarily a sexually transmitted disease. Injection drug use transmission occurs when contaminated injection equipment is used. Perinatal transmission can occur in utero, during delivery, or postnatally via breastfeeding.

6. HIV-gingivitis differs from gingivitis in the unaffected patient in which of the following ways?
   a) no differences
   b) gingivitis in the non-HIV infected individual is usually seen with poor oral hygiene, whereas HIV-gingivitis can be seen with excellent oral hygiene
   c) gingivitis in the non-infected individual is usually associated with extreme bone loss while HIV-gingivitis is associated with tooth decay
   d) gingivitis is harder to treat in the patient without HIV infection

b) Gingivitis in the non-HIV infected individual is usually seen with poor oral hygiene, whereas HIV-gingivitis can be seen with excellent oral hygiene. For this reason, gingival lesions exhibiting signs consistent with gingivitis in the absence of local irritants that do not respond to conventional periodontal therapy, may be associated with HIV infection.

7. Which of the following is ***not*** a treatment option for the HIV-gingivitis patient?
   a) scaling and root planing (if necessary)
   b) broad spectrum antibiotics
   c) close follow-up and maintenance
   d) prescription for Peridex rinse

b) Broad spectrum antibiotics: Antibiotics are not indicated for treatment of HIV-gingivitis. Metronidazole is part of the treatment for HIV-associated periodontitis.

8. Treatment for HIV-periodontitis includes gross debridement with 10% betadine irrigation with follow-up evaluation for scaling and root planing.
   a) True b) False

a) True

9. Topical creams used for treatment of angular chelitis include:
   a) Mycelex cream (Clotrimazole)
   b) Lidocaine gel
   c) Topical acyclovir
   d) all of the above

a) Angular chelitis is a fungal infection and an antifungal cream would be the treatment of choice.

10. Which of the following signs/symptoms/information are consistent with herpes zoster?
   a) pain
   b) unilateral appearance
   c) incidence increases with age
   d) oral vesicles that rupture to form ulcers
   e) all of the above

e) All of the above: All of the answers are possible signs/symptoms/information regarding herpes zoster.

11. Kaposi's sarcoma most often presents as a benign lesion.
   a) True b) False

b) False: KS is a malignant lesion. The most common site for KS is the palate; the gingiva are the second most common, but KS may be found anywhere in the oral cavity.

12. What percent of oral cancers seen by dentists are squamous cell carcinomas?
    a) 30%
    b) 50%
    c) 70%
    d) 90%

d) 90%

13. Which of the following lesions are of most concern when encountered in the oral cavity?
    b) white only
    b) red-white combined
    b) red only

c) Red only: Red lesions found in the oral cavity are of most concern because they are most likely to be malignant lesions. The percentages of lesions being malignant upon initial biopsy are as follows: leukoplakias 6%, erythroleukoplakias 14%, erythroplakias 51%.

14. Heavily keratinized areas such as gingiva, hard palate, and dorsum of tongue are the most common locations for squamous cell carcinoma.
    a) True b) False

b) False: Intraoral squamous cell carcinoma is most commonly found on the lateral or ventral tongue, floor of the mouth, lips, and soft palate.

15. Although stress and mechanical irritation are associated with aphthous ulcers, the true etiology remains unknown.
    a) True b) False

a) True: The etiology for aphthous ulcers is not known.

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AIDS RESOURCES

AEGIS (AIDS Education Global Information System) *www.aegis.com*
The world's largest HIV knowledge base, featuring all the best newsletters, HIV news from top newspapers and wire services, and search capability for all documents.

AIDS.org *www.aids.org*
This global network provides up-to-date information and links to HIV-focused web sites.

AIDS Clinical Trials Information Service *www.actis.org*
Provides current information on clinical trials, study protocols, study locations, patient enrollment and eligibility, study results, and database searches.
In Canada and the United States
1-800-TRIALS-A (1-800-874-2572)

AIDS InfoNet *www.aidsinfonet.org*
Provides fact sheets on treatments, prevention, social services, and web resources. Easy to print, appropriate for patient and clinician education, and updated on a regular basis. Available in English and Spanish.

American Foundation for AIDS Research (AmFAR) *www.amfar.org*
Provides information about basic science research, clinical research and information, and public policy programs.
(212) 806-1600

CDC National Prevention Information Network *www.cdcnpin.org/*
A national reference, referral, and distribution service for HIV-related information. Services include comprehensive reference and referral services, publications distribution services, resource centers, free on-line and Internet services, clinical trials information and HIV/AIDS treatment information. CDC NAC FAX is a 24-hour, on-demand service that quick faxes documents and other information. Available documents include HIV Prevention Fact Sheets, MMWRs, global and domestic AIDS surveillance statistics, Spanish language materials and other resources.
1-800-458-5231

The Dental Alliance for AIDS Care *www.critpath.org/daac*
Website for an international organization of dental health providers. Includes information on Ryan White Care Act, continuing education, and resources.

Healthcare Consortium *www.hivcme.org*
The Healthcare Consortium is a non-profit organization that provides educational programming through conferences and on its web page. Areas of interest include women and HIV, adolescent issues, HIV in prisons, and treatment issues.

HIV/AIDS Treatment Information Service (ATIS) *www.hivatis.org*
Information about federally approved HIV/AIDS treatment options and links to other key HIV/AIDS information resources. All calls are confidential. Offered by the US Public Health Service.
1-800-HIV-0440 (1-800-448-0440)

HIV Dent *www.hivdent.org*
Several sections on the oral manifestations of HIV disease and a large picture gallery. Also, information on infection control, post-exposure protocols, pediatric/adolescent care, medications, funding, and other resources.

HIV InSite *www.hivinsite.org*
Sponsored by the University of California at San Francisco. The site provides excellent search capabilities in a broad spectrum of science, prevention, and treatment arenas.

HIV Telephone Consultation Service for Health Care Providers *www.ucsf.edu/hivcntr*
A national HIV telephone consultation service for clinicians who have questions about HIV care practices. Physicians, nurse practitioners, and pharmacists from San Francisco General Hospital staff the consultation line. It is a useful resource for clinicians practicing in areas where HIV expertise is not readily available.
1-800-933-3413

National Clinicians' Post-Exposure Prophylaxis Hotline (PEPline) *www.ucsf.edu/hivcntr*
A 24-hour hotline providing prompt and up-to-date information for clinicians who need advice on treating health care workers who have suffered occupational exposures to blood borne pathogens. On-line information on post-exposure prophylaxis information is available on PEPnet.
1-800-HIV-4911 (1-800-448-4911)

National Minority AIDS Council (NMAC) *www.nmac.org*
A national AIDS organization that develops programs and services for community-based organizations serving people of color affected by HIV/AIDS. Programs include: U.S. Conference on AIDS, research and treatment information, and technical assistance to health departments and community planning groups.
(202) 483-6622 (202)-438-NMAC

National Native American AIDS Prevention Center *www.nnaapc.org*
An organization providing information on HIV and related diseases among American Indians, Alaska natives, and native Hawaiians.
(510) 444-2051

National Pediatric and Family HIV Resource Center *www.pedhivaids.org*
Provides material concerning the care of children and families living with HIV, current fact sheets on HIV in women and children, catalog of available books and videos.
1-800-362-0071

Project Inform *www.projinf.org*
An HIV treatment information organization working on behalf of people living with HIV infection. Provides information on treatment, research and advocacy issues. Operates the Project Inform National HIV/AIDS Treatment Hotline. Staffed by volunteers who confidentially answer questions about HIV treatment and related diseases.
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