



## Diagnosis and treatment of viral infections

Sol Silverman, Jr, MA, DDS<sup>a,\*</sup>, Craig S. Miller, DMD, MS<sup>b</sup>

<sup>a</sup>*Department of Stomatology, University of California School of Dentistry, Box 0422 S-612, 513 Parnassus Avenue, San Francisco, CA 94143, USA*

<sup>b</sup>*Department of Oral Medicine, Microbiology, Immunology, and Molecular Genetics, University of Kentucky College of Dentistry, College of Medicine, MN-118, Lexington, KY 40536-0297, USA*

Viral infections are of concern to dental professionals because of ease of transmission, the oral, latent, recurrent, and systemic diseases they can produce, their association with opportunistic infections and malignant transformation, and their influence on infection control. In this article, information regarding the following viruses is provided: (1) HIV, (2) human herpesviruses, (3) human papillomaviruses, (4) enteroviruses, and (5) hepatitis C virus.

### HIV

We are currently in the third decade of an RNA virus pandemic. There are approximately 40 million people throughout the world infected with HIV. It is estimated that more than 16,000 new infections occur each day. HIV is spread predominantly by sexual contact, blood or blood products, or perinatal exposure. Infection also results from high-risk activities, such as sharing needles with infected drug users, having unprotected sexual activity with one or more infected partners, receiving infected blood or blood products, or being accidentally exposed to infected materials.

In the United States, almost 500,000 persons are reported to be living with HIV and AIDS. More than 2 million persons are believed to be infected, however. Approximately 98% of infections occur in adults and adolescents, and approximately one third of new cases occur in women. New infections are

occurring at a disproportionately higher rate in African Americans. In reversal since the late 1990s, the number of new cases and deaths is increasing once again because of viral resistance to multiple drug therapy, apathy toward barrier techniques, the increasingly large number of individuals living with HIV who serve as a reservoir for transmission, and widespread drug abuse and prostitution.

The HIV epidemic is an important concern to the dental profession for many reasons. First, infection control measures are required in the dental office. Second, many oral and systemic manifestations occur in immunocompromised individuals who have falling numbers of physiologically incompetent lymphocytes and rising viral loads. Third, recognition of the signs and symptoms of HIV infection should lead to referral of the patient to a physician for diagnostic testing.

Acute HIV infection in most cases produces flu-like symptoms that develop 2 to 6 weeks after the initial infection. Soon thereafter, persistent generalized lymphadenopathy occurs, which is followed by a latent phase. Initially the latent phase is asymptomatic. Later as the viral loads rise and the CD4<sup>+</sup> cell count drops, lymphadenopathy, weight loss, fever, diarrhea, fatigue, skin anergy, neurologic decline, parotid enlargement, and opportunistic infections develop. Many of the numerous oral lesions that develop are caused by increased individual susceptibility to viral transmission and proliferation. These infections, which involve the herpes family viruses and human papillomaviruses, are more prevalent in HIV-seropositive patients and are usually concurrent and recurrent. An increasing number of HIV patients are coinfecting with the hepatitis C virus.

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\* Corresponding author.

E-mail address: [ssjr@itsa.ucsf.edu](mailto:ssjr@itsa.ucsf.edu) (S. Silverman).

The final stage of the disease (AIDS) is often marked by fatal respiratory infections, lymphoma, or cancer. Treatment involves the use of highly active antiretroviral agents, such as nucleoside, nucleotide, and nonnucleoside reverse transcriptase inhibitors, and protease inhibitors, which are used in combination to block virus replication and maturation.

### Human herpesviruses

The human herpesvirus (HHV) family includes herpes simplex viruses (HSV-1 and -2), varicella-zoster virus (VZV, HHV-3), Epstein-Barr virus (EBV, HHV-4), cytomegalovirus (CMV, HHV-5), lymphotropic viruses (HHV-6 and -7), and Kaposi's sarcoma virus (HHV-8). These large DNA viruses have the hallmark of establishing latent infection. The latent infection serves as a reservoir for the periodic activation of virus. Although the molecular factors that regulate activation of HHVs are still undefined, aging, immunosuppression, stress, and tissue damage predispose HHVs to reactivation. Reactivation occurs despite cell-mediated and humoral HHV immunity. Clinical manifestations are diverse and are more severe during immunosuppression.

#### *Herpes simplex viruses*

HSV-1, the most common of the HHV oral infections, must contact mucosa or abraded skin to initiate infection. By puberty, most individuals have been

exposed to HSV and have developed circulating antibodies. The virus incubates and replicates for 2 to 12 days within epithelium and then penetrates local nerve endings [1]. After the primary infection, the virus travels to regional ganglia, where it remains latent indefinitely. Asymptomatic shedding and reactivation are common [2]. Although population studies are variable, clinical recurrences are estimated to occur in up to 40% of cases [3].

More than 67% of initial exposures are asymptomatic subclinical infections [4]. The remaining individuals who acquire the primary infection experience marked signs and symptoms that last up to 2 weeks (Fig. 1). Features include gingivostomatitis, lip vesicles and coalescing ulcerations, fever, lymphadenopathy, and oropharyngeal pain. Approximately 10% of adults are not exposed to or do not obtain adequate level of antibodies. These persons are at risk for developing adult-onset acute herpetic gingivostomatitis. Although the signs and symptoms in adults are usually more severe, the attack is usually complete in 2.5 weeks. The initial HSV infection incurs permanent immunity from a similar future attack; however, it does not prevent reactivation and recurrent mucosal and labial flares.

Recurrent mucosal (intraoral herpes) and labial (cold sores) infections create a lifetime problem in persons who are susceptible to reactivation of latent HSV (Fig. 2). These lesions recur near the point of entry into the body and are usually caused by HSV-1, although HSV-2 (usually associated with genital herpes) occasionally can be identified. The signs,



Fig. 1. Primary adult-onset herpetic gingivostomatitis in a 28-year-old man. It was manifested by sudden onset, pain, fever, lymphadenopathy, and gingivitis. There had been no similar previous attacks, and the signs and symptoms resolved completely in 2 weeks.



Fig. 2. Typical recurrent oral herpes manifested by irregular, shallow gingival ulcerations that tend to coalesce and usually resolve within 7 to 10 days. The lesions are often mistaken for trauma.

symptoms, and treatment are similar for both serotypes. Lesions are often preceded by prodromal symptoms of burning, tingling, itching, or pain.

Recurrent intraoral HSV is often mistaken for some form of traumatic injury, because lesions appear on periosteal bound mucosa as small, irregular, erosive areas or ulcers that usually disappear within 1 week. An important implication is transmission, because vesicular and ulcerative lesions shed virus during the first 2 to 3 days, during which time HSV can be transmitted. Common sites of spread are the eye (herpetic keratitis) and fingers (herpetic whitlow) (Fig. 3). “Cold sores” are a problem because of aesthetics, pain, and source of transmission. The nature of HSV recurrences varies and often is preceded by stress, irritation, exposure

to sunlight, cold, fever, trauma, and immunosuppression [5–7]. There are reports that HSV infection can precede, or be subclinically involved in, an attack of erythema multiforme, which indicates a possible antigenic role [8].

Diagnosis of HSV infections is usually based on the history and clinical findings. Cultures, cytologic smears that show multinucleation, and special immunofluorescent processing can be helpful when clinical recognition is uncertain. Serologic diagnosis is of value only to determine past exposure.

Definitive treatment includes the use of systemic or topical antiviral drugs [9–12] (Table 1). Precursor antiviral agents, such as valacyclovir and famciclovir, have better oral bioavailability than acyclovir and penciclovir. If not used early in the infection (first 3 to



Fig. 3. Herpetic whitlow of the finger contracted by contact with a cold sore.

Table 1  
Antiviral drugs

Generic (trade name)		Suggested dosage (days) <sup>a</sup>
Systemic:	acyclovir (Zovirax)	400 mg 3 × daily (7)
	famciclovir (Famvir)	125 mg 1 × daily (5)
	valacyclovir (Valtrex)	500 mg 2 × daily (5)
Topical:	acyclovir (Zovirax)	5% ointment
	penciclovir (Denavir)	1% cream
	docosanol (Abreva)	10% cream (over-the-counter)

Apply topical medications to oral lesions at least four times daily.

<sup>a</sup> Dosage levels are adjusted according to clinical severity and response. For severe infection: acyclovir 5–10 mg/kg IV q8h for 7–10 days, famciclovir 500 mg t.i.d., or valacyclovir 1000–2000 mg b.i.d. For acyclovir-resistant cases: foscarnet (Foscavir) 40–60 mg/kg IV q8h for 7–10 days, or cidofovir (Vistide) 5 mg/kg.

4 days), antiviral drugs are usually ineffective. Antiseptic, analgesic, and antiinflammatory medications can be beneficial in reducing pain and transmission of the disease. Systemic antiviral agents are used in complicated primary infections, HSV infections in the immunocompromised, prophylaxis for seropositive patients who undergo chemotherapy or transplantation, HSV-associated central nervous system disease, and recurrent erythema multiforme. Systemic antiviral agents are used often as daily prophylaxis. Nephrotoxicity, although rare, is a concern with the use of high-dose systemic acyclovir, valacyclovir, and famciclovir, particularly if patients have renal insufficiency.

### Epstein-Barr viruses

Epstein-Barr virus is associated with infectious mononucleosis, hairy leukoplakia, nasopharyngeal carcinomas, and lymphomas [13]. The primary infection, referred to as infectious mononucleosis, usually causes a sore throat, fever, cervical lymphadenopathy, malaise and pain, and occasional hepatosplenomegaly. It occurs chiefly in adolescents and young adults. The disease is of low contagiousness, and transmission is through exchange of EBV-contaminated saliva. Affected patients often demonstrate multiple petechiae located on the soft palate or lips. The lymphadenopathy is often bilateral and affects the posterior cervical nodes. Blood studies reveal atypical lymphocytes, heterophile antibodies, and mildly elevated transaminase levels. Treatment in most cases is palliative and supportive. Recovery usually occurs within 1 to 2 months; however, the virus enters latency in lymphocytes.

Epstein-Barr virus is associated with hairy leukoplakia, which is a benign manifestation of epithelial hyperplasia and hyperkeratosis that primarily occurs on the lateral border(s) of the tongue. It appears as a corrugated white lesion that does not rub off (Fig. 4). Hairy leukoplakia is predominately seen in individuals infected with HIV; however, it may be seen in non-HIV immunosuppressed patients. Hairy leukoplakia is almost always asymptomatic, with the principal significance being a sign of immunosuppression.

The diagnosis of hairy leukoplakia is clinically suggestive and can be confirmed by biopsy. Cytologic scrapings are somewhat characteristic by featuring nucleoprotein condensations in nuclei. Treatment is elective and includes high-dose antiviral drugs, topical podophyllin in 25% tincture of ben-



Fig. 4. Hairy leukoplakia in an HIV-positive patient. The lesion was asymptomatic and chronic.



Fig. 5. A lytic bone lesion caused by lymphoma.

zoin, or laser vaporization. Recurrence is common. Although the term “leukoplakia” has been used to describe the condition, there is no known associated precancerous risk.

Epstein-Barr virus is well known for its ability to cause lymphocyte immortalization and malignant transformation [13,14]. Such transformation occurs in a small percentage of infected persons. The transformation process is complex and involves the upregulation of several viral and host gene products and immunosuppression [13,15]. Critical is the upregula-

tion of EBV latency membrane protein 1 and the NF- $\kappa$ B pathway that alters apoptotic and growth pathways [16]. EBV-associated lymphomas in the head and neck region present as nontender swellings in Waldeyer’s ring, cervical lymph nodes, salivary glands, oral mucosa, and lytic bone lesions (Fig. 5). Persistent fever of unknown cause, weight loss, malaise, sweating, and abdominal or chest pain often accompany the condition. Radiation and chemotherapy are used for treatment. Of interest is the recent detection of EBV DNA in the serum of patients who have nasopharyngeal carcinoma, certain lymphomas, and gastric carcinoma.

#### *Cytomegalovirus*

Cytomegalovirus rarely causes mouth lesions but can be associated with persistent mucosal ulcerations (Fig. 6) in transplant patients and immunosuppressed persons. Transmission is person-to-person mainly through sexual and blood contacts. The primary infection in most persons goes unrecognized. In utero and perinatal transmission can lead to deafness, learning disabilities, and mental retardation, however. CMV enters latency in peripheral blood mononuclear cells and reactivates during immunosuppression. CMV infection recurs commonly in HIV-infected individuals and presents as pneumonitis, retinitis, or nervous system disease [17]. CMV can infect and replicate in major salivary glands, particularly in immunocompromised patients, which can lead to swelling, pain, and xerostomia, secondary to lymphocytic salivary gland infiltrates.

The diagnosis of CMV infection is established by special stains and immunoprocessing (polymerase

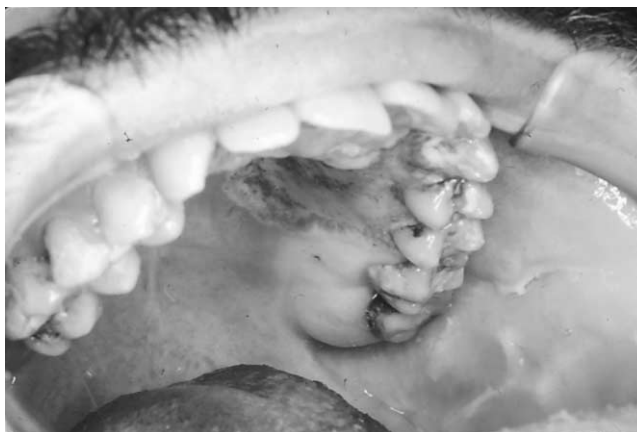


Fig. 6. A painful ulceration of the palate of 1 month duration in an HIV-positive patient. Biopsy showed this to be a CMV-induced lesion that responded to high-dose antiviral medication.

chain reaction) of biopsy specimens and specific serologic antibody tests. Successful treatment is based on establishing the diagnosis and the use of antiviral agents, such as acyclovir or ganciclovir.

#### *Herpes varicella virus or varicella-zoster virus*

Varicella-zoster virus is well known for causing chickenpox. It is a highly contagious virus that is generally spread during the late winter and spring months to young children who lack antibodies against varicella-zoster virus. After exposure and a 2- to 3-week incubation period, mild prodromal features appear. The first recognizable signs are fever, malaise, and a distinctive red, itchy truncal rash. The rash spreads quickly to the neck, face, and extremities and is followed shortly by the eruption of papules that form vesicles and pustules. Occasionally, oral inflammatory vesicular-ulcerative lesions develop that may be seen on the posterior palate or buccal mucosa. Anorexia, chills, fever, nasopharyngitis, and musculoskeletal aches may accompany the disease. Lesions heal within 7 to 10 days as patient antibody titers rise and control the infection. Complications such as pneumonitis and encephalitis are infrequent.

Varicella-zoster virus resides latently in the sensory ganglia of the host after the initial infection. The virus reactivates in approximately 0.2% of adults, more often in elderly and immunosuppressed patients and has an increasing incidence with age. The recurrent attack is known as “herpes zoster” or “shingles.” The disease is preceded by hypersensitive skin overlying the area of attack. Within a few days, the classic manifestations are painful vesicles that occur unilaterally along nerve dermatomes. Most commonly,

lesions occur on the trunk between vertebrae T3 and L2 and on the face along the ophthalmic division of the trigeminal nerve and extend up to the midline (Fig. 7). In immunocompetent patients, vesicles break down, scab, and resolve within 2 to 4 weeks.

The diagnosis of varicella-zoster virus infection is made by history, clinical findings, and serology. Polymerase chain reaction is used for diagnosis in severe cases that may involve the central nervous system [18]. Treatment involves antiviral drugs in high dosages (acyclovir, 4000 mg/d in divided doses; famciclovir, 1500 mg/d in three divided doses; valacyclovir, 3000 mg/d in two divided doses) given within the first week [19]. Supportive treatment for pain and pruritus is also in order. The most painful and discouraging complication is postherpetic neuropathy, which can be debilitating. Early use of corticosteroids along with antiviral treatment may help minimize, or even prevent, the neuropathy. Longer standing cases benefit from the use of amitriptyline, nortriptyline, topical lidocaine patches, and gabapentin, which should be considered early in the course of treatment [20,21]. A live-attenuated vaccine (Varivax) virus is currently available for the prevention of chickenpox.

#### *Human herpesvirus-6 and -7*

Human herpesvirus-6 and -7 are T-cell lymphotropic herpesviruses that have significance in dentistry. Like most human herpesviruses, they are ubiquitous and capable of establishing a lifelong, latent infection in humans. HHV-6 is particularly efficient at infecting infants and young children and produces exanthem subitum (roseola) and febrile



Fig. 7. Varicella (herpes) zoster or “shingles” in a 65-year-old patient. Note the unilateral distribution. The vesicles/ulcers formed scabs and healed after 3 weeks. Treatment was supportive and included high-dose acyclovir.

seizures. HHV-6 is present in saliva [22] and has been detected in salivary glands and tonsillar tissue [23]. Primary infection in adults can cause a mononucleosis-like illness. The virus is harbored during latency in peripheral blood mononuclear cells, salivary glands, mucosa, and tonsils [23]. Reactivation occurs in the immunocompromised host and is associated with fever, leukopenia, encephalitis, interstitial pneumonitis, skin rash, and bone marrow suppression. A role for HHV-6 in malignant transformation remains to be defined, although HHV-6 can transactivate other viruses, such as human papillomavirus (HPV), associated with malignant disease [24].

Human herpesvirus-7 is associated with exanthem subitum and febrile seizures and is detected in the saliva of healthy adults [25]. HHV-7 infection generally occurs later in childhood after infection with HHV-6. Case reports suggest that HHV-7 may reactivate after immunosuppression or the flu and can cause encephalitis, encephalopathy, and febrile convulsions [26].

#### *Human herpesvirus -8 (Kaposi's sarcoma herpesvirus)*

Human herpesvirus-8 is a sexually transmitted herpesvirus that infects endothelial cells. A secondary source of infection is organ transplantation [27]. Up to 15% of the US adult population is infected [28,29]. Kaposi's sarcoma herpesvirus contains several viral oncogenes, and Kaposi's sarcoma is the primary disease associated with its infection [30]. Primary effusion lymphoma and multicentric Castleman's disease also have a strong association with this virus [31].

Kaposi's sarcoma is a pseudomalignancy that has a particularly high prevalence in immunocompromised patients, homosexual men infected with HIV,

and elderly persons. It attacks many different organs and is usually multifocal. Kaposi's sarcoma does not metastasize but can be the cause of death. It occurs most commonly in the skin, with the mouth being the second most common site. Within the mouth, the palate and gingiva are common sites. Kaposi's sarcoma is highly vascular and typically appears purple-red. The initial appearance of Kaposi's sarcoma is a purplish macule that enlarges to become a violaceous papule or nodule. Lesions are single or multifocal, can cause discomfort and bleeding, and can impact appearance (Fig. 8).

Since the institution of "high activity anti-retroviral therapy", the occurrence of Kaposi's sarcoma has been much less frequent. Treatment involves low-dose radiation, chemotherapy (systemic or intralésional), and surgery.

#### **Human papillomavirus**

Human papillomaviruses are small, double-stranded, non-enveloped DNA viruses that have a propensity for infecting epithelium. Approximately 5.5 million new HPV infections occur every year in the United States, and 10% to 33% of sexually active individuals are infected with the virus. Current estimates indicate that 10% to 18% of adults carry HPV, with the highest rates of infection found in 19- to 26-year-old individuals.

There are more than 100 types of HPV, and at least 45 types are known to infect genital and oral epithelium. HPVs can be harbored latently within epithelium for the life of the host, undergo a lytic infection and alter epithelial cell growth and replication, or dysregulate the cell cycle, which results in



Fig. 8. Nodular Kaposi sarcoma of the palate in a patient with AIDS whose CD4 count was less than 200/mm<sup>3</sup>.

pre-malignant changes. Infection outcomes depend on the infecting HPV genotype, anatomic site, and immune response. Benign genotypes (HPV 6, 11, 44, 55) replicate in the lower epidermis and differentiated cells (keratinocytes) and produce increased numbers of epithelial cells and koilocytosis. High-risk genotypes [16,18,31,33,35] are associated with pre-malignant and malignant epithelial disease.

Low-risk HPV types are associated with benign proliferations, such as the squamous papilloma, verruca vulgaris, condyloma acuminatum (venereal warts), and focal epithelial hyperplasia (Heck's disease). The squamous papilloma is a well-defined, pink-white, exophytic and pedunculated or stalk-like mass. This small, usually asymptomatic growth may occur on any mucosal surface.

Condyloma acuminata intraorally appear as small verrucous lesions of varying sizes or they can mimic small fibromas. Condyloma acuminata occur on any mucosal surface and may be single or multiple, clustered or coalesced, and widespread (Fig. 9). Condylomas are more commonly seen in immunocompromised patients and are transmitted by oral sex. A higher prevalence of oral condyloma in HIV-positive patients on antiretroviral drugs compared to HIV-positive patients not on antiretroviral drugs has been reported. Reports have shown a decreased occurrence of most other HIV-associated oral lesions, however, since high-activity antiretroviral therapy was initiated.

The common skin wart (verruca vulgaris) is a rare intraoral finding. It is most often seen on the commissures of the lips in children and adolescents and is caused by autoinoculation. Occasionally it occurs on the tongue, labial mucosa, or gingiva. Warts have

a rough, pebbly, clefted surface and a well-demarcated border.

Focal epithelial hyperplasia is a multipapular condition associated with HPV-13 and -32 infection that was originally reported in Native American Indians and Eskimos. The infection is transmitted by kissing. The HPV-induced, small, flat papules occur on labial and buccal mucosa and tongue. Lesions coalesce and develop a cobblestone-like surface.

Benign HPV lesions can enlarge and spread or resolve spontaneously; however, most do not regress without treatment. Ablative and chemotherapeutic approaches are useful. Surgery, laser treatment, and cryotherapy have good success in removing HPV proliferations when the basal and adjacent epithelium is removed. High-speed evacuation is recommended during laser surgery to prevent aspiration of viral DNA that might be contained within the plume. A useful topical pharmacologic approach involves podofilox 0.5% (Condylox, Oclassen), an agent that causes necrosis by arresting cells in mitosis. It is applied twice daily for 3 days followed by no treatment for the next 4 days; then the cycle is repeated up to four times. Immunomodulatory approaches include intralesional interferon, imiquimod (Aldara) 5% cream at bedtime three times per week for up to 16 weeks (alters cell cytokines and stimulates interferon production), and cimetidine (a histamine receptor antagonist), 30 mg/kg body weight (bw), given daily in divided doses usually over 8 weeks. Recurrence is seen in approximately 10% to 25% of patients generally within 3 months. Sexual partners should be examined and treated to minimize the risk of transmission and recurrences.



Fig. 9. Condyloma acuminatum associated with the human papillomavirus in a sexually active homosexual man. Treatment was by laser surgical removal.

Infection with high-risk HPV types has an association with precancerous oral leukoplakia and squamous cell carcinoma. In one form of leukoplakia, proliferative verrucous leukoplakia, HPV-16 has been identified frequently. This finding helps explain the high rate of malignant transformation associated with proliferative verrucous leukoplakia. It can be characterized clinically as a progressive leukoplakic lesion that can vary from somewhat corrugated and flat to one that is exophytic and verrucous. Proliferative verrucous leukoplakia may have a red component and a variable microscopic presentation that ranges from hyperkeratosis and epithelial dysplasia to carcinoma. It may be asymptomatic, cause slight discomfort, or be painful. The lesion usually involves more than one mucosal surface. It occurs four times more often in women than men and occurs less commonly in smokers than nonsmokers. In one long-term study [32], more than half of proliferative verrucous leukoplakias were reported to have transformed into carcinoma less than 8 years after diagnosis.

Human papillomavirus can be detected in approximately 30% of oral squamous cell carcinoma cases, which suggests that the virus may play a causative role, similar to its role in anogenital carcinoma [33]. The role of HPV in oral cancer seems different from the carcinogenic effects of tobacco and alcohol. For example, HPV-positive oropharyngeal cancers occur less often among moderate to heavy alcohol drinkers and tobacco smokers. Patients in this category also have improved survival from cancer when compared with HPV-negative head and neck squamous cell carcinoma [34]. The role of HPV in carcinogenesis may involve binding to p53 suppressor protein, which in turn enhances epithelial cell proliferation and neoplasia.

Diagnosis of HPV-infected mucosa is based on the history, clinical findings, and cellular characteristics seen in biopsy specimens (koilocytes). Confirmation can be made by immunohistochemistry, in situ hybridization, or polymerase chain reaction processing. Currently, specific identification and typing are complex and expensive. There is no effective vaccine, and antiviral medications do not eliminate latent infection. The most effective treatment is by surgical approaches and behavior modification (eg, barrier techniques). In the future, HPV analyses may prove important for directing treatment, such as by gene therapy.

### Enteroviruses

Enteroviruses are single-stranded, small RNA positive-sense, nonenveloped viruses that cause a spectrum of human disease. The family includes polioviruses, coxsackieviruses (23 serotypes), echoviruses (32 serotypes), human enteroviruses 68 to 71, hepatitis virus A, and several nonhuman enteric viruses that are well known for causing foot-and-mouth disease in livestock. Most nonpolio enteroviruses infect nasopharyngeal cells and inhabit the alimentary (enteric) tract. They are transmitted by ingestion (fecal-oral route) and contaminated saliva of close contacts in poor sanitary environments and warm climates. Many enterovirus infections are endemic in Southeast Asia [35].

The bulk of enterovirus infections are benign and self-limiting, manifested mostly by fever alone [36]. The primary enterovirus infections that involve the oropharyngeal complex are hand-foot-and-mouth disease and herpangina. These infections occur primarily in children. Hand-foot-and-mouth disease is caused

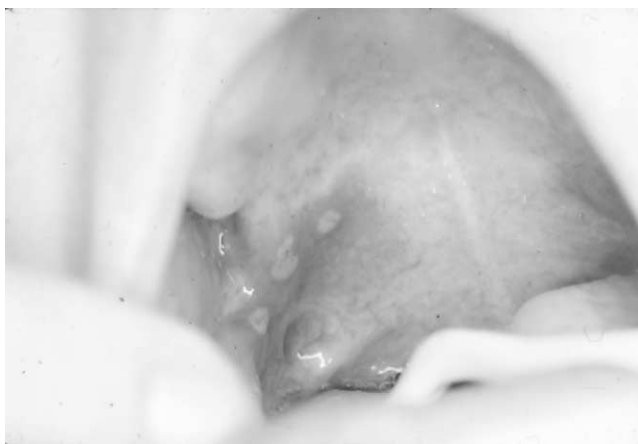


Fig. 10. Oropharyngeal ulcers associated with coxsackievirus infection.



Fig. 11. Erosive lichen planus of the buccal mucosa developed in a patient who previously had been diagnosed as hepatitis C virus positive. A cause-and-effect relationship has not been proved conclusively.

by various members of the Coxsackie group and enterovirus 71. They produce oral ulcerations and extraoral “rashes” of the hands and feet (Fig. 10). Herpangina, caused by group A and sometimes group B coxsackieviruses, has the main feature of erythema and multiple vesicles of the oropharynx and posterior tongue. Both conditions are accompanied by pain, fever, headache, lymphadenopathy, and malaise. Infection by nonpolio enteroviruses can produce lymphonodular pharyngitis, which is manifested mainly by nonulcerative oropharyngeal nodules, abdominal pain, vomiting, conjunctivitis, and croup. Serious infections can result in meningitis, encephalitis, paralysis, myocarditis, hepatitis, and death. Although there is no viral latency, patients can become reinfectd by one of the many serotypes.

The diagnosis of enteroviral infection can be made by viral culture, serology, and nucleic acid amplification [36]. Treatment for self-limiting oropharyngeal enterovirus infections in immunocompetent individuals is supportive and palliative. Immunoglobulin, interferon- $\alpha$ , and the antiviral agent pleconaril are available for treatment of persons with meningitis and an immunocompromised status [37].

### Hepatitis C virus

Hepatitis C virus (HCV) is a small, single-stranded RNA virus of the *Flaviviridae* family that was previously known as one of the non-A/non-B hepatitis viruses. Infection by HCV is a widespread global disease. In the United States, it is estimated that 4 million Americans are infected and potential carriers of HCV, with 30,000 new infections and 10,000

deaths each year [38]. Transmission is highest among drug users, who share HCV-contaminated needles, and persons who have large or repeated percutaneous exposures. Of individuals infected, approximately 80% develop hepatitis, and 10% to 20% of those persons develop cirrhosis. Treatment involves combination chemotherapy and liver transplantation.

Dental implications relate to the need for bodily fluid borne–pathogen control in the dental office, demand for proper sterilization and disinfection protocols, and use of barrier techniques to protect against contaminated blood and saliva. HCV has been detected in saliva [39]; however, it is less infectious than hepatitis B virus. HCV carriers often are not aware of their seropositive status.

Many questionable reports [40] indicate a relationship between HCV infection and oral lichen planus. Although this occurrence has not been documented conclusively, there seems to be an unexplainable risk that may not be coincidental. Because oral lichen planus can be a source of oral pain and interfere with oral functions, its diagnosis and treatment are important considerations. The diagnosis of oral lichen planus is based its on clinical characteristics (Wickham striae, erosions, ulcers) and biopsy (Fig. 11). Effective treatment requires the elimination of drugs that can cause similar appearing lichenoid eruptions, followed by the use of topical or systemic corticosteroids.

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