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Oral herpetic infections (HSV 1–8)

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There are 80 known herpesviruses, and at least eight of them are known to cause infections in humans. These include herpes simplex virus (HSV) 1 and 2, varicella zoster virus (VZV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), human herpes virus 6 (HHV-6), human herpes virus 7 (HHV-7), and human herpes virus 8 (HHV-8). There are structural and behavioral characteristics that are common to the members of the herpesvirus family. All herpes viruses contain four layers: an inner core of double-stranded DNA, a protein capsid, the tegument, and a lipid envelope containing glycoproteins derived from the nuclear membrane of host cells [1]. Herpes viruses cause a primary infection when the patient initially contacts the virus and then remain latent within the nuclei of specific cells for the life of the individual. The site of latency differs among the herpesviruses. HSV 1, HSV 2, and VZV remain latent in the sensory nerve ganglia; CMV remains latent in lymphocytes and possibly in salivary gland tissue; EBV remains latent in B lymphocytes and salivary gland tissue; and HHV-6 and HHV-7 remain latent in CD4 lymphocytes [1]. HHV-8 also remains latent; although the exact site of latency is still unknown, it is most likely associated with B lymphocytes circulating in the hematopoietic system [1]. After reactivation, herpesviruses can cause localized symptomatic or asymptomatic recurrent infections. They are transmitted from host to host by direct contact with saliva or genital secretions. HHV-8 may be transmitted by organ transplantation [2]. Herpesviruses are shed in the saliva of asymptomatic hosts, who act as constant reservoirs for new primary infections in previously uninfected individuals. Herpes viruses are known to transform cells in tissue culture. EBV has been associated with malignancies in humans, such as

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nasopharyngeal carcinoma and B-cell lymphomas. Other malignancies are associated with EBV, including a nasal T-cell/NK cell lymphoma seen most commonly in South East Asia [3]. HHV-8 has been definitively linked to malignant processes, such as Kaposi's sarcoma, to several lymphoproliferative disorders, and to Castleman's disease [2].

Herpes simplex virus

HSV 1 and HSV 2 are the two major types of HSV and are the causative agents in most common intraoral herpesvirus infections. They can be distinguished by the distinct antibodies that are formed against each type of virus or by analysis of the nuclear DNA by restriction endonuclease analysis [4]. Classically, HSV 1 causes a majority of cases of oral and pharyngeal HSV infection, meningoencephalitis, and dermatitis above the waist; HSV 2 is implicated in most genital and anal infections [1]. Depending on sexual practices, both types can cause primary or recurrent infections in the oral or genital area [1]. HSV infections of the finger (herpetic whitlow) develop after contact with infected saliva or bronchial secretions.

Primary herpes simplex infections

The incidence of primary infections with HSV 1 increases after 6 months of age because of the loss of anti-HSV antibodies acquired from the mother during gestation. The incidence of primary HSV 1 infection reaches a peak between 2 and 3 years of age [4]. Primary HSV 1 infections may still occur in adolescents and adults, with occasional cases being reported in patients over 60 years of age [5]. The incidence of primary HSV 2 infection does not increase until sexual activity begins.

A significant percentage of primary herpes infections are subclinical or cause a pharyngitis difficult to distinguish from other upper respiratory viral infections. Symptomatic primary HSV disease is preceded or accompanied by generalized symptoms that may include fever, headache, malaise, nausea, and vomiting. These prodromal symptoms are important to consider when clinically differentiating HSV infections from other mucocutaneous diseases. Lymphadenopathy may be evident as well. In the oral cavity, vesicles and ulcers appear on the oral mucosa, and generalized acute marginal gingivitis occurs 1 to 2 days after the prodromal symptoms appear (Fig. 1). Primary HSV in healthy children is usually a self-limiting disease with fever disappearing in 3 or 4 days and oral lesions healing in a week to 10 days.

Treatment of primary HSV infection is usually palliative. Milder cases can be managed by supportive care only, including maintenance of fluids, use of acetaminophen to reduce fever, and use of topical anesthetics such as viscous lidocaine or a mixture of liquid diphenhydramine, milk of magnesia, and carafate (magic mouthwash) to decrease oral pain [1]. If the patient presents

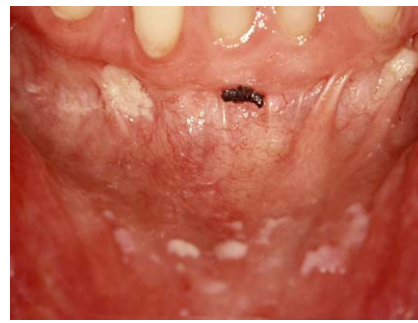

Fig. 1. Primary HSV infection. Note areas of ulceration on gingiva and labial mucosa. There is an area of hemorrhagic crusting on the gingiva due to ulceration.

to the clinician within 72 hours of onset of vesicle eruption, antiviral medication may be helpful in decreasing healing time of the lesions by inhibiting DNA replication in HSV infected cells [6]. Acyclovir has been shown to decrease symptoms of primary HSV infection in children, including days of fever and viral shedding [7]. Newer antiherpes drugs are available, including valacyclovir and famciclovir. The newer drugs have increased bioavailability allowing effective treatment with fewer daily doses [8] (Table 1).

Recurrent herpes simplex infection

Following resolution of a primary HSV infection, the virus migrates to the trigeminal nerve ganglion, where it is capable of remaining in a latent state. Reactivation of virus may follow exposure to cold, exposure to sunlight, stress, trauma, or immunosuppression and cause a recurrent infection [9]. Recurrent herpes labialis (RHL) is the common form of recurrent oral HSV infection that appears on the vermilion border or skin of the lip and is referred to as a "cold sore" or "fever blister" (Figs. 2 and 3) [1]. Recurrent herpes infections in otherwise healthy patients should be treated symptomatically. Treatment, as well as chronic suppression of severe, painful, or deforming recurrent herpes, may require systemic antiviral medications (Tables 2 and 3).

Table 1
Recommended dosages of antiviral medication for treatment of primary herpes simplex virus infections*

	Acyclovir	Valacyclovir
Dose	200 mg	1000 mg
Frequency	5×/day	2×/day
Duration	10 days	10 days

* These guidelines are based on Food and Drug Administration–approved treatment recommendations of genital herpes.

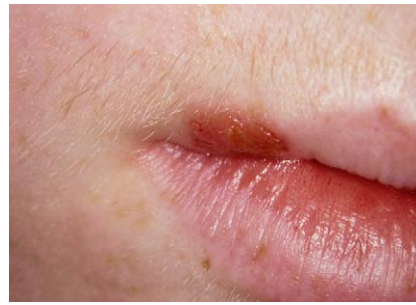

Fig. 2. Acute recurrent herpes labialis.

Studies comparing topical antiviral medications for treating RHL have been published [10,11]. Topical penciclovir reduces the duration and pain of RHL by 1 to 2 days [12]. The recommended dosage of topical penciclovir is application to the area every 2 hours for 4 days while awake. Acyclovir, as well as *N*-Docosanol cream, also is currently available for topical use. Topical acyclovir has been reported to decrease duration of RHL lesions by 12 hours and found to be more effective than *N*-Docosanol in treating RHL [10,13]. Overall, the benefit of applying these medications to RHL lesions seems to be limited and does not significantly decrease the duration of lesions as compared with topical penciclovir [10]. Recently, topical resveratrol, a phenol compound that is produced naturally and commonly found in grapes, has been shown to be useful in treating cutaneous HSV infections in mice [14]. Although it has not been compared with topical penciclovir, it has been shown to be as effective as topical acyclovir and to be more effective than *N*-Docosanol in infected mice [14]. Some clinicians advocate the use of suppressive doses of systemic acyclovir to prevent severe, frequent, and disfiguring recurrences of RHL.

Although a majority of recurrent herpes occurs on the lips and heavily keratinized mucosa of the palate and gingiva, recurrent intraoral herpes (RIH) can occur on any intraoral mucosal surface and is seen most frequently in immunocompromised patients. (Fig. 4) [4]. Patients at high risk for severe

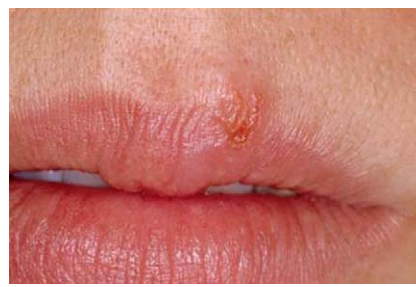

Fig. 3. Healing recurrent herpes labialis. (Courtesy of Andres Pinto, DMD, Philadelphia, PA.)

Table 2
Recommended dosages of antiviral medication for treatment of recurrent herpes simplex virus infections

	Acyclovir[a]	Valacyclovir[a,b]	Famciclovir[a,c]
Dose	200 mg	500 mg	125 mg
Frequency	5×/day	2×/day	2×/day
Duration	5 days	3 days	5 days

[a] These guidelines are based on Food and Drug Administration–approved treatment recommendations of genital herpes.

[b] Recommended treatment for herpes labialis is 2000 mg, 2×/day, for 1 day.

[c] For patients with HIV disease with recurrent orolabial or genital herpes, the dosage of famciclovir is 500 mg, 2×/day, for 7 days.

recurrences are those receiving cancer chemotherapy or immunosuppressive drugs to prevent graft rejection after transplantation and patients with advanced AIDS [1]. Recurrent HSV lesions in immunocompromised patients appear as progressively enlarging ulcers, which may involve large portions of the labial, intraoral, genital, or rectal mucosa if left untreated [15]. These lesions occasionally disseminate, causing generalized infection; therefore, it is imperative for clinicians to rule out HSV as a cause of oral vesicles or ulcers in immunosuppressed individuals [1].

Immunosuppressed patients with HSV infection respond well to acyclovir administered orally or intravenously [16]. Occasional cases of acyclovir-resistant HSV have been reported; foscarnet, another antiviral drug, has been effective therapy for these patients [17]. Valacyclovir should be used with caution for immunosuppressed patients because of the potential risk of hemolytic uremic syndrome.

Recurrent HSV has been known to trigger episodes of erythema multiforme. HSV is presently believed to be the most common cause of recurring episodes of erythema multiforme in susceptible individuals who develop an immune response to HSV [1]. Patients who get severe recurring erythema multiforme from HSV commonly receive prophylactic doses of

Table 3
Recommended dosages of antiviral medication for chronic suppression of recurrent herpes simplex virus

	Acyclovir[a]	Valacyclovir[a,b,c]	Famciclovir[a]
Dose	400 mg	500 mg	250 mg
Frequency	2×/day	1×/day	2×/day
Duration	Up to 1 year	Up to 1 year	Up to 1 year

[a] These guidelines are based on Food and Drug Administration–approved treatment recommendations of genital herpes.

[b] For patients with greater than 9 episodes of recurrence per year, the dosage of valacyclovir is 1000 mg, 1×/day.

[c] For patients with HIV disease and CD4 count $\geq$ 100 cells/mm^3, the dosage of valacyclovir is 500 mg, 2×/day.

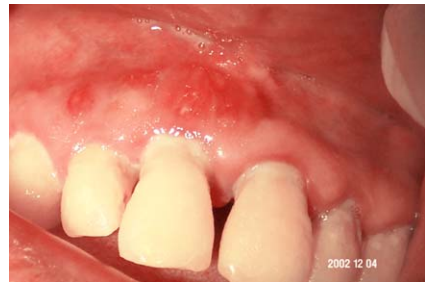

Fig. 4. Recurrent intraoral herpes on gingival tissue. (Courtesy of Juan F. Yepes, DDS, MD, Philadelphia, PA.)

antiviral medication to prevent recurrence. The recommended prophylaxis doses are the same as for suppression of genital herpes.

Diagnosis

Differential diagnosis

The majority of HSV infections are diagnosed clinically; however, a differential diagnosis should be formulated that includes other mucocutaneous diseases. Recurrent aphthous stomatitis is commonly misdiagnosed as an HSV infection; however there are certain clinical features that are unique to each disease. HSV typically has a prodrome of fever and malaise before vesicle and ulcer eruption; recurrent aphthous stomatitis generally does not have the same prodromal symptoms before ulcer formation. HSV infections usually present with associated gingival erythema, which is uncommon with recurrent aphthous stomatitis.

HSV infections may appear clinically similar to coxsackie viral infections, the most common being herpangina and hand-foot-and-mouth disease. Herpangina can be differentiated from HSV infection because lesions associated with herpangina are typically confined to the posterior oropharynx, including the soft palate, uvula, tonsils, and pharyngeal wall. In contrast, HSV lesions may appear throughout the entire oral cavity. Herpangina infections are usually milder than HSV infections, generally occur in epidemics, and do not cause a generalized acute gingivitis like that associated with primary HSV infection [4]. Hand-foot-and-mouth disease can also present with oral ulcerations and can be differentiated from HSV infection on the basis of lesions involving the hands and feet.

Erythema multiforme may also be considered in the differential diagnosis of HSV infections. Distinguishing features of an erythema multiforme infection include intraoral lesions with a wide range of clinical presentations and typically associated target lesions on the skin. In contrast, HSV lesions tend to be more uniform and consistent in clinical presentation. In addition,

erythema multiforme lesions do not typically appear on the gingival tissue or cause gingival erythema, which are characteristic features of HSV infections.

Laboratory diagnosis

Laboratory tests may be necessary to diagnose atypical presentations of HSV infections. These tests should be used when evaluating immunocompromised patients with atypical lesions.

Virologic tests

The standard for virus identification and diagnosis is isolation in tissue culture. The goal of virus isolation is to observe cytopathic effects of the cells inoculated with virus. Cytopathic effects are the degenerative changes that cells undergo when infected with virus. The rate at which cytopathic effects develop depends on the type of host cell, the type of virus, and the concentration of virus [18]. When viewed at high power using light microscopy, virally infected cells demonstrate multinucleated giant cells, syncitium, and ballooning degeneration of nuclei.

Cytology smears

A smear taken of epithelial cells at the base of a suspected lesion may be studied to determine if epithelial cells show changes consistent with HSV infection. The most common stain used is Giemsa, and virally infected cells demonstrate the same characteristics demonstrated by virologic testing. When a Papanicolaou's stain has been performed, eosinophilic intranuclear viral inclusion bodies (Lipschutz or Cowdry type A) can be seen.

Immunomorphologic tests

The diagnosis of herpesvirus infections can be made more quickly and accurately by using immunomorphologic techniques [19]. In the direct fluorescent assay (DFA), the specimen is incubated with fluorescein isothiocyanate–labeled HSV type-specific monoclonal antibody [20]. The positively infected cells are fluorescent green when examined under a fluorescent microscope. This technique can be used for the rapid diagnosis of a clinical specimen, the identification of virus in tissue culture displaying cytopathic effect, and the typing of recovered HSV isolates from tissue culture [21]. Studies have concluded the overall sensitivity when using DFA techniques to detect HSV is 80%, the specificity is 98% to 100%, and the positive predictive value ranges from 90% to 100% [22,23].

Serologic tests

Serologic tests are completed to detect antibody formation in a patient's blood sample. They are useful in diagnosing a primary HSV infection:

a fourfold or greater antibody rise in convalescent serum is required for the diagnosis of a primary infection. If serology is used in the diagnosis of suspected HSV infection, an acute specimen should be obtained within the initial 3 days of the infection, and a convalescent specimen should be obtained approximately 4 weeks later. Because of the delayed humoral response, antibodies are not present in the acute specimen but appear during convalescence. This test may provide useful retrospective information but is of little help when managing a patient in the acute phase of illness.

Varicella zoster virus

VZV is responsible for two major clinical infections: the primary type is chickenpox (varicella), and the recurrent type is shingles (herpes zoster [HZ]).

Varicella

Chickenpox is characteristically a benign illness of children spread by direct contact with either the skin lesions or nasopharyngeal secretions of an infected individual [1]. The incubation period is 10 to 21 days, and patients are infectious for approximately 1 week after symptoms begin. Complications of chicken pox include pneumonitis and Reye's syndrome, a progressive encephalopathy that most frequently occurs in children who have been given aspirin during an acute varicella infection [24].

Skin lesions of chickenpox are characterized by maculopapular lesions that are intensely pruritic. The lesions rapidly develop into fluid-filled vesicles on an erythematous base. Oral lesions may be present that resemble vesicles or ulcers seen in primary HSV, but these lesions are not a particularly important symptomatic, diagnostic, or management problem [4].

Herpes zoster

After primary infection, VZV becomes latent in dorsal root or cranial nerve ganglia. In 0.3% to 0.5% of the population, the virus becomes reactivated, causing HZ [1]. The nerves most commonly affected with HZ are C-3, T-5, L-1, and L-2. When HZ involves the trigeminal ganglion, the first division (ophthalmic or V_1) is most commonly involved, and eye involvement becomes a potentially serious complication [1]. Consultation with an ophthalmologist is necessary in these cases.

The initial symptoms of HZ are pain, tenderness, and paresthesia along the course of the affected nerve. Unilateral vesicles appear 3 to 5 days later on an inflamed base along the involved nerve (Fig. 5). When the geniculate ganglion of the facial nerve is infected, characteristic signs include unilateral vesicles of the external ear and oral mucosa as well as unilateral facial paralysis, a group of signs referred to as Ramsay-Hunt syndrome [1]. HZ may also occasionally affect motor nerves.

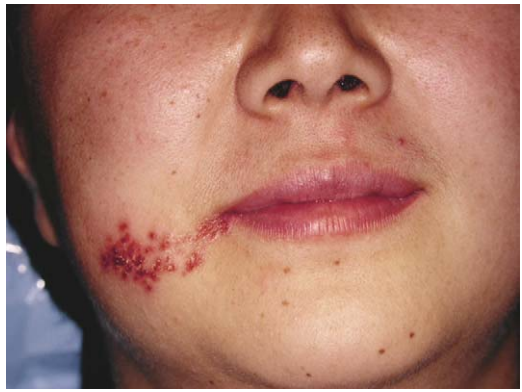

Fig. 5. Herpes zoster infection involving the mandibular branch (V3) of the trigeminal nerve.

Approximately 15% to 20% of the cases of HZ of the trigeminal nerves affect either the maxillary division (V_2) or mandibular division (V_3), leading to pain, unilateral facial lesions, and intraoral lesions along the course of the affected nerve [4]. Diagnosis of HZ is usually based on characteristic clinical signs and symptoms. Intraoral lesions caused by HZ usually demonstrate a dramatic unilateral distribution associated with intense pain, helping distinguish it from an HSV recurrence [25]. VZV may cause pain without lesions developing along the course of the nerve. This manifestation is called ''zoster sine herpete'' or ''zoster sine eruptione'' [4]. Atypical presentations may require laboratory testing for confirmation of VZV. These methods include viral cultures, cytology smears, immunomorphologic techniques, and serologic testing, as previously described.

Immunocompromised patients with HZ are at risk for developing life-threatening infections. In this population, HZ may cause large local lesions or disseminated infection. Oral HZ in immunosuppressed patients has been reported to cause necrosis of alveolar bone and exfoliation of teeth [4]. Disseminated infections among immunocompromised individuals may include widespread skin lesions, meningitis, encephalitis, VZV pneumonia, and hepatitis.

Antiviral agents, such as acyclovir, are effective in shortening the course of HZ, accelerating healing, and reducing acute pain [4]. Valacyclovir and famciclovir have been reported to be more effective than acyclovir for treating HZ [4] (Table 4).

Table 4
Recommended dosages of antiviral medication for treatment of herpes zoster

	Acyclovir	Valacyclovir	Famciclovir
Dose	800 mg	1000 mg	500 mg
Frequency	5×/day	3×/day	3×/day
Duration	7–10 days	7 days	7 days

Postherpetic neuralgia (PHN) is a potential consequence of HZ resulting from scarring of the involved nerve during infection [1]. PHN is a painful, sometimes debilitating condition that can last months to years after the lesions are healed. The incidence of PHN is increased in patients older than 50 years, and use of valacyclovir or famciclovir has been advocated to reduce the incidence and duration of PHN [26]. According to some investigators, the use of a short course of systemic corticosteroids decreases the incidence of PHN, but the usefulness of this recommendation is disputed [1]. Other effective therapies for treatment of PHN are gabapentin, topical capsaicin, and tricyclic antidepressants [4].

Cytomegalovirus

Cytomegalovirus is a frequent cause of asymptomatic infection in humans and may cause significant clinical disease in immunosuppressed patients [27]. The virus is mainly transmitted by contaminated blood and bodily secretions, including breast milk, saliva, and genital fluids [1].

Neonates may develop cytomegalic inclusion disease, a congenital form of CMV infection. In its most severe form, this disease is associated with microcephaly, chorioretinitis, nerve deafness, hepatitis, hepatosplenomegaly, and thrombocytopenia [27]. In immunocompromised adults, salivary gland enlargement is a common finding with this disease [1].

In healthy children and adults, primary CMV infection is usually asymptomatic. This primary CMV infection results from either blood transfusions or sexual contact in a previously seronegative person [1]. Clinical symptoms include fever, myalgia, cervical lymphadenopathy, and mild hepatitis. Tonsillopharyngitis is much less common than in primary EBV infection, and lymphadenopathy and splenic enlargement are less prominent features [26]. Complications of primary CMV infection may include myocarditis, pneumonitis, and aseptic meningitis.

CMV infection may produce serious disease and death in immunosuppressed patients who have deficiencies of cell-mediated immunity. Patients at risk for developing life-threatening CMV infections are solid-organ and bone marrow transplant recipients, as well as patients with HIV infection. Forty percent of patients with advanced HIV disease develop sight-threatening or life-threatening disease caused by CMV [27]. CMV retinitis is characterized by hemorrhagic retinal necrosis spreading along retinal vessels and threatening sight when disease encroaches on the macula [28]. The widespread use of antiretroviral therapy has reduced the incidence of complications caused by CMV infection; however, a newly recognized syndrome consequent to the use of highly active antiretroviral therapy has been described [1]. This new variant, immune recovery vitritis, has been reported in patients with inactive previously treated CMV retinitis as the CD4 count reconstitutes on antiretroviral therapy [29].

There are reports of CMV-related oral lesions in AIDS patients. They have been described as slowly enlarging ulcers [30]. One study reported that CMV was the sole ulcerogenic viral agent in a majority of oral lesions in a study population of AIDS patients [31]. Coinfection of oral ulcers with both HSV and CMV also has been reported in AIDS patients [31,32]. Reports indicate that genomes of CMV are frequently detected in several different types of periodontal disease [33].

The diagnosis of CMV disease is made by histologic evaluation of suspected lesions, viral culture, antigen detection, and CMV DNA detection [34]. Biopsy specimens of CMV lesions demonstrate characteristic histopathologic changes, including enlarged cells with prominent intranucleolar and intracytoplasmic inclusions, referred to as "owl-eye" cells [1]. Viral culture of suspected lesions is used to detect CMV, but a major drawback is the prolonged length of time required for a positive culture to develop. Polymerase chain reaction (PCR) techniques are becoming the standard assay for detecting CMV in most laboratories. PCR can detect CMV in body fluids such as urine, blood, and saliva [1]. Salivary gland enlargement used to be a major clinical criterion for identifying CMV infection in infants because of the tendency of CMV to infect salivary glands [1].

One study indicated a relationship between xerostomia and the presence of CMV in saliva of HIV-infected individuals [35]. Prospective studies using viral culture, PCR techniques, and histopathologic examination demonstrated a significant correlation of xerostomia with presence of CMV in the saliva [36]. The results of this study suggest a link between CMV in saliva and salivary gland dysfunction in HIV-infected patients.

Antiviral agents are used to treat CMV infections. Drugs such as ganciclovir, foscarnet, and cidofivir have been shown to be effective in treating CMV infections [27]. Newer drugs, including valganciclovir, maribavir, and tomeglovir, are currently in development for the treatment of CMV infections [37].

Epstein-Barr virus

EBV is a herpesvirus that preferentially infects B lymphocytes. Infection of humans with EBV usually occurs by contact with oral secretions. The virus replicates in cells of the oropharynx, and nearly all seropositive persons actively shed virus in the saliva [38]. Whereas most EBV infections of infants and children are asymptomatic or have nonspecific symptoms, infections of adolescents and adults frequently result in infectious mononucleosis [39,40]. Infectious mononucleosis from EBV has an incubation period of up to 8 weeks [1]. The initial symptoms consist of a triad of symptoms: fever, lymphadenopathy, and pharyngitis. Splenomegaly, hepatomegaly, oral ulcers, and palatal petechiae also may be present, and the cervical lymph nodes are involved in more than 90% of patients [1]. Less common complications include hemolytic anemia, thrombocytopenia, aplastic anemia, splenic rupture, and

encephalitis [39]. The disease is usually self limiting, and most patients are well within 1 month.

Various malignancies are associated with EBV, including nasopharyngeal carcinoma, Burkitt's lymphoma, Hodgkin's disease, and lymphoproliferative disease [1]. Burkitt's lymphoma is a high-grade malignant lymphoma of small, noncleaved B cells. In Africa, tumors of Burkitt's lymphoma usually present in the jaw, and more than 90% of these cases are associated with EBV [38].

Oral hairy leukoplakia is caused by EBV and occurs in a large percentage of HIV-infected patients as well as in some immunosuppressed transplant recipients [38]. It presents as a raised, white, corrugated lesion of the oral mucosa that commonly involves the lateral or ventral surfaces of the tongue. It may also appear as a plaquelike lesion and is often seen bilaterally. Multiple strains of EBV DNA may be present in the lesions [1].

Human herpes virus 6

HHV-6 was discovered in 1986 when it was isolated from peripheral blood lymphocytes of six individuals with lymphoproliferative disorders [41]. Studies revealed that CD4 T cells were the major type of cell infected by HHV-6 [42,43]. Two variants of HHV-6 have been differentiated: HHV-6A and HHV-6B.

Primary infection with HHV 6 can be asymptomatic, cause an unspecified febrile illness, or present as a specific clinical disorder, roseola (exanthema subitum) [44]. The virus is commonly isolated from saliva, and respiratory transmission is the major route of primary infection. HHV-6B is the particular subtype associated with roseola [45]. HHV-6A is the subtype commonly reactivated in AIDS patients [43] and has also been postulated as a cofactor in the progression of HIV disease [46]. Oral lesions are not commonly associated with either HHV-6A or -6B infections.

Human herpes virus 7

HHV-7 was discovered in 1990 when the virus was isolated from activated CD4 T cells obtained from a healthy individual. The genomes of HHV-7 and both variants of HHV-6 are closely related, with 20% to 75% nucleic acid homology depending on the genes being compared [44].

Primary infection with HHV-7 is most often asymptomatic; however, it may cause a roseola-like illness. HHV-7 is commonly isolated from saliva, and the mode of transmission is analogous to that of HHV-6 [4].

Reactivation of HHV-7 in immunocompromised patients can lead to widespread multiorgan infection, including encephalitis, pneumonitis, and hepatitis [44]. HHV-6 can be activated from latency by HHV-7 reactivation [47,48]. Oral lesions are not commonly associated with HHV-7 infections.

Human herpes virus 8

HHV-8 was isolated in tumor tissue from a patient with AIDS-associated Kaposi's sarcoma in 1994 and was named Kaposi sarcoma herpesvirus (KSHV) [49]. Moritz Kaposi, a Hungarian-born dermatologist, first described idiopathic multiple, pigmented sarcoma of the skin in 1872 and suggested a possible infectious origin for Kaposi's sarcoma [44].

Like EBV, KSHV is capable of inducing malignant tumors in humans. Of the KSHV-associated malignant diseases, the most prominent is Kaposi's sarcoma. HIV-associated Kaposi's sarcoma can be aggressive, and lesions may become more widespread and prominent, involving oropharyngeal and gastrointestinal mucous membranes [49]. Most intraoral Kaposi's sarcoma lesions are found on the hard and soft palates with a typical clinical appearance of reddish-purple macules or nodules. Extrapalatal lesions may be seen on the gingiva and tongue; these lesions are associated with a more rapid progression of Kaposi's sarcoma and with HIV disease [50].

Summary

Knowledge of the clinical manifestations of herpes virus infections will enable the clinician to formulate a proper differential diagnosis of oral soft tissue lesions and plan the appropriate therapeutic strategy to manage the disease. Clinicians should be aware of the potentially critical nature of herpes infections in immunocompromised patients, and aggressive treatment should be pursued for these individuals.

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